BEFORE THE
SCIENTIFIC AND MEDICAL ACCOUNTABILITY
STANDARDS WORKING GROUP
OF THE INDEPENDENT CITIZENS' OVERSIGHT COMMITTEE
TO THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE
ORGANIZED PURSUANT TO THE
CALIFORNIA STEM CELL RESEARCH AND CURES ACT

REGULAR MEETING

LOCATION: MIYAKO HOTEL
1625 POST STREET
SAN FRANCISCO, CALIFORNIA

DATE: MAY 9 & 10, 2007

REPORTER: BETH C. DRAIN, CSR
CSR. NO. 7152

BRS FILE NO.: 78260 & 78261

I N D E X

SAN FRANCISCO, CALIFORNIA; WEDNESDAY, MAY 9, 2007

04:09 P.M.

CHAIRMAN LO: WELL, WELCOME EVERYONE. WHY DON'T WE COME ON AND GET STARTED. IT'S REALLY GREAT TO SEE EVERYBODY. I MUST SAY I'M DELIGHTED THAT YOU ALL COULD COME, AND IT'S REALLY WONDERFUL TO SEE EVERYONE AGAIN.

I'D LIKE TO OFFICIALLY CALL US TO ORDER, TO WELCOME YOU TO SAN FRANCISCO, TO TELL THOSE OF YOU FROM OUT OF TOWN THAT HAD YOU COME YESTERDAY OR THE DAY BEFORE, IT WOULD HAVE BEEN ABOUT 90 DEGREES AND REMIND YOU OF THE EAST COAST. BUT THIS IS TYPICAL WEATHER. IT MAY CLEAR UP A BIT, BUT THE FOG WILL KEEP YOU COOL.

I REALLY DO WANT TO WELCOME YOU AND FIRST JUST SAY THAT SHERRY LANSING, MY CO-CHAIR, CAN'T BE HERE TODAY. SHE'S AT A CANCER FUND-RAISER. SHE WANTED ME PARTICULARLY TO SAY THAT THAT WAS THE ONLY DAY THAT THE OTHER PEOPLE COULDN'T MAKE IT, AND SHE'S EXTREMELY SORRY THAT SHE COULDN'T BE HERE. AND I'M ACTUALLY SORRY AS WELL BECAUSE AS I WAS GOING TO SAY SOME VERY NICE THINGS ABOUT THE AWARD SHE RECEIVED AT THE ACADEMY AWARDS SOME MONTHS AGO WHERE SHE WAS GIVEN A LIFETIME ACHIEVEMENT AWARD, THE JEAN HERSHOLT HUMANITARIAN AWARD. AND IT WAS REALLY WONDERFUL.

I HAVE AN 11-YEAR-OLD DAUGHTER WHO MANY OF YOU HAVE HEARD ABOUT IN THE COURSE OF THESE MEETINGS. SHE'S VERY MUCH THE SHE'S COOL; SHE'S NOT IMPRESSED. SHE ACTUALLY WATCHED. "WOW, THAT'S AN IMPRESSIVE WOMAN." I SAID YES. SO JUST A TIP OF THE HAT TO SHERRY LANSING.

I ALSO WANT TO SORT OF WELCOME BACK SOME PEOPLE.

DR. PRIETO: HELLO.

CHAIRMAN LO: HI. WHO IS THIS?

DR. LOMAX: CAN YOU HEAR US?

DR. PRIETO: YES, I CAN. IS THAT GEOFF?

CHAIRMAN LO: FRANCISCO, HI. IT'S BERNIE LO. WE'RE JUST GETTING STARTED. WELCOME. SORRY YOU CAN'T BE HERE, BUT GREAT TO HAVE YOU ON THE PHONE.

I JUST WANTED TO SAY --

DR. PRIETO: BERNIE, YOUR VOICE IS A LITTLE SOFT. CAN YOU GET CLOSER TO THE MICROPHONE? MUCH BETTER.

CHAIRMAN LO: SORRY. I JUST WANT TO SAY A COUPLE THINGS. FIRST, I WANT TO PARTICULARLY WELCOME JANET ROWLEY BACK. I KNOW SHE'S HAD SOME HEALTH PROBLEMS, AND IT'S WONDERFUL TO SEE YOU AGAIN. JOSE CIBELLI FROM MICHIGAN STATE, WHO, AS YOU KNOW, STEPPED DOWN FROM OUR PANEL WHILE HE ACTUALLY ASKED HIS

UNIVERSITY TO HOLD AN INVESTIGATION BECAUSE HE WAS ONE OF THE CO-AUTHORS OF THE HWANG PAPER. HE ACTUALLY ASKED MICHIGAN STATE TO CARRY OUT AN INVESTIGATION. THAT HAS BEEN COMPLETED, AND THE MICHIGAN STATE COMMITTEE DETERMINED THAT THERE WAS NO -- THAT JOSE AND HIS LAB WERE NOT RESPONSIBLE FOR ANY OF THE EGREGIOUS MISCONDUCT IN THAT STUDY. AND SO HE'S BEEN CLEARED, AND HE IS GOING TO BE REJOINING THE COMMITTEE, AND WE'RE CERTAINLY GLAD FOR THAT. HE HAD TO SPEND A LOT OF TIME TO CLEAR HIS NAME, BUT I'M GLAD HE DID SO.

DR. PRIETO: VERY GOOD.

CHAIRMAN LO: OTHER THINGS. AS MANY OF YOU KNOW, ZACH HALL HAS STEPPED DOWN AS PRESIDENT OF CIRM. HE WAS PLANNING TO RETIRE ANYWAY TO HIS FARM IN WYOMING, AND THEN HE HAS HIMSELF SOME HEALTH PROBLEMS THAT ARE GOING TO REQUIRE SOME SURGERY. AND HE STEPPED DOWN EARLY. I JUST WANT TO SORT OF AGAIN A TIP OF THE HAT AND THANKS TO ZACH, THAT I THINK HE GOT CIRM OFF TO A TERRIFIC START. AND I REALLY PERSONALLY FOUND IT WONDERFUL TO WORK WITH HIM, AND THAT HE REALLY DID WANT NOT JUST THE BEST CUTTING EDGE SCIENCE, BUT THE HIGHEST ETHICAL STANDARDS AND SUPPORTED THIS COMMITTEE AND I KNOW DID A LOT OF BEHIND-THE-SCENES WORK WITH GEOFF AND SCOTT AND OTHER OF THE STAFF TO MAKE SURE THAT OUR DELIBERATIONS WERE UNDERSTOOD BY THE ICOC. SO, AGAIN,

THANKS TO ZACH, AND WE'LL ALL DESCEND ON HIM IN HIS FARM SOMETIME IN WYOMING.

FINALLY, KEVIN EGGAN IS NOT ON THE CALL, BUT I THINK GEOFF ACTUALLY SENT AROUND AN ARTICLE HIS GROUP PUBLISHED IN *NATURE* AND *NEUROSCIENCE* ON USING EMBRYONIC STEM CELLS TO CREATE SCNT-TYPE LINES. AND HE HAS A LINE NOW WITH THAT EXPRESSES THE ALS GENOTYPE, BUT NOT USING OOCYTES, BUT USING THE CYTOPLASM DERIVED FROM EMBRYONIC STEM CELLS. SO THIS IS A POSSIBLE REALLY EXCITING ADVANCE SCIENTIFICALLY.

AND THEN, FINALLY, I GUESS I WANT TO CALL THIS -- THERE'S CONFLICT OF INTEREST HERE. I SIT ON THE COUNCIL AT IOM. SO ONE OF THE THINGS I LIKE TO DO IS TELL WHAT NICE THINGS IOM AND NAS DID. AND THERE WAS AN UPDATE OF THE 2005 NATIONAL ACADEMIES GUIDELINES FOR HUMAN EMBRYONIC STEM CELL RESEARCH. AND ACTUALLY IT TRACKS VERY CLOSELY WITH OUR CIRM REGULATIONS, AND I THINK REALLY HELPS TO ESTABLISH THE WORK WE DID AS SORT OF A SET OF GUIDING PRINCIPLES.

DR. PRIETO: BERNIE, MY SIGNAL IS FADING OUT.

CHAIRMAN LO: EVERY TIME I TURN AWAY, I'M AFRAID YOU END UP NOT HEARING ME. SO YOU ALL HAVE ELECTRONIC COPIES; AND IF ANYONE WANTS A HARD COPY OF THIS, I THINK WE CAN PROBABLY GET THEM FOR YOU.

SO I THINK THIS IS A TIME WHERE I THINK WE

CAN SORT OF SIT BACK. A NUMBER OF US WERE TALKING AHEAD OF TIME THAT WE'VE DONE A LOT OF GOOD WORK. I THINK THE REGULATIONS THAT WE WORKED SO HARD ON ARE NOW FINAL REGULATIONS. IN ADDITION, CIRM HAS DONE GOOD WORK. THEY'VE APPROVED, I THINK IT'S, 158 MILLION NOW IN GRANTS AT 23 INSTITUTIONS.

MR. SHEEHY: ABOUT A HUNDRED FIFTY.

CHAIRMAN LO: THE MONEY IS FLOWING. I THINK, YOU KNOW, THE RESEARCH NOW WILL START TO HOPEFULLY REALLY, REALLY TAKE OFF. THERE'S AN ONGOING SET OF SCIENTIFIC AND GRANTS MAKING RESPONSIBILITIES, BUT IT WILL ALL BE DONE IN COMPLIANCE WITH OUR REGULATIONS. WE'LL HEAR MORE ABOUT THE GRANTS ADMINISTRATION TOMORROW MORNING.

SO DO WE NEED A FORMAL ROLL CALL? IS THAT WHAT WE NEED TO DO AT SOME POINT?

DR. LOMAX: YES. WE SHOULD DO THE ROLL CALL, AND I WILL NOW INITIATE THE ROLL CALL.

MARCY FEIT. ROBERT KLEIN. SHERRY LANSING. FRANCISCO PRIETO.

DR. PRIETO: HERE.

DR. LOMAX: JEFF SHEEHY.

MR. SHEEHY: HERE.

DR. LOMAX: JONATHAN SHESTACK. ALTA CHARO. BERNARD LO.

CHAIRMAN LO: HERE.

DR. LOMAX: PATRICIA KING.

MS. KING: HERE.

DR. LOMAX: TED PETERS.

DR. PETERS: HERE.

DR. LOMAX: JOSE CIBELLI. KEVIN EGGAN. ANN KIESSLING. JEFFREY KORDOWER. KENNETH OLDEN.

DR. OLDEN: HERE.

DR. LOMAX: JANET ROWLEY.

DR. ROWLEY: HERE.

DR. LOMAX: ROBERT TAYLOR.

DR. TAYLOR: HERE.

DR. LOMAX: JOHN WAGNER. JAMES WILLERSON.

CHAIRMAN LO: THANKS.

DR. LOMAX: WE HAVE BEEN INFORMED THAT ANN KIESSLING IS EN ROUTE FROM THE AIRPORT, BUT SHE HAS BEEN DELAYED. SHE SHOULD BE JOINING US IN THE NEXT HOUR.

CHAIRMAN LO: FOGGY DAYS MEAN YOUR FLIGHTS GOING HOME MAY NOT TAKE OFF ON TIME. SORRY TO SAY. GEOFF, COULD I CALL ON YOU FOR A STAFF REPORT.

DR. LOMAX: LET ME KNOW. WE'RE GETTING A TINY BIT OF A FEEDBACK HERE, SO WE'RE GOING TO BACK DOWN ON THE AMPLIFICATION A TINY BIT.

DR. PRIETO: MY SIGNAL SEEMS FINE NOW.

DR. LOMAX: AGAIN, I'D LIKE TO ECHO BERNIE'S WELCOME. IT IS GOOD TO SEE EVERYONE AGAIN, AND IT'S NICE TO BE ABLE TO REFLECT A LITTLE BIT ON THE WORK WE'VE DONE AND THINK A BIT ABOUT WHAT WE'LL BE DOING IN THE FUTURE. IT WAS A LITTLE BIT OF A TRACK MEET THERE FOR THE FIRST SIX MEETINGS OF THE WORKING GROUP.

WHAT I'D LIKE TO DO IS A SHORT, A VERY SHORT PRESENTATION TO GET US UP TO SPEED ON WHAT WE'VE DONE OVER THE -- AND THERE ARE A FEW PIECES OF THE REGULATION THAT ARE STILL OUT THERE IN THE PROCESS. SO JUST ORIENT EVERYONE WHERE WE ARE. THIS IS OUR HISTORIC TIMELINE, WHICH I HOPE YOU'RE ALL FAMILIAR WITH.

WE HAD FIVE WORKING GROUP MEETINGS OVER A SIX-DAY PERIOD TO DRAFT OUR REGULATIONS, AND THE VAST MAJORITY OF THAT WORK WAS DONE IN 2005. WE ALSO HAD THE PUBLIC WORKSHOPS AND A MEETING WITH THE INSTITUTIONAL WORKSHOPS IN DECEMBER OF THAT YEAR. THIS ALL CULMINATED WITH THE ICOC APPROVAL OF OUR INITIAL DRAFT OF THE REGULATIONS IN FEBRUARY 2006.

DR. PRIETO: GEOFF, IS THIS THE POWERPOINT?

DR. LOMAX: YEAH. DO YOU HAVE THAT ONE? I'M NOT SURE YOU DO ACTUALLY.

DR. PRIETO: THIS IS NOT THE OVERVIEW OF THE NATIONAL ACADEMIES ONE?

DR. LOMAX: NO.

DR. PRIETO: OKAY.

DR. LOMAX: I COULD HAVE FORWARDED THAT TO YOU, BUT THIS IS JUST THAT TIMELINE THAT WE'VE HISTORICALLY USED TO TALK ABOUT OUR WORK PLAN. BEAR WITH US. HOPEFULLY IT WILL MAKE SENSE ORALLY. THERE'S NOTHING TERRIBLY COMPLICATED HERE.

DR. PRIETO: OKAY.

DR. LOMAX: AFTER THE ICOC APPROVAL, WE SUBMITTED THE ACTUAL REGULATORY PACKAGE WHICH WE, THE COLLECTIVE WE, SCOTT, I THINK, WAS REALLY RESPONSIBLE FOR A TREMENDOUS EFFORT THERE OF TAKING THE REGULATIONS AND PUTTING IT INTO A FORMAT IN WHICH THE OFFICE OF ADMINISTRATIVE LAW WOULD APPROVE AND ALLOW US TO INITIATE OUR RESPONSIBILITIES UNDER THE ADMINISTRATIVE PROCEDURE ACT.

SO ON MARCH 17TH WE HAD AN INITIAL ROUND OF PUBLIC COMMENTS. WE RECEIVED CONSIDERABLE VOLUME OF PUBLIC COMMENTS IN THAT MARCH THROUGH MAY PERIOD. AND THEN IF YOU WILL REMEMBER, WE HAD A SERIES OF TELEPHONE MEETINGS TO RESOLVE ISSUES THAT CAME UP AS A RESULT OF PUBLIC COMMENTS. WE MADE MODIFICATIONS TO LANGUAGE IN THE REGULATIONS, AND THEN WE REFERRED -- WE HAD, IN FACT, FOUR ITERATIONS WHERE WE PUT IT OUT TO COMMENT, GOT SOME COMMENTS, MADE SOME CHANGES, PUT IT BACK OUT

TO COMMENT, MADE SOME ADDITIONAL CHANGES, OUT AGAIN, FINALLY BACK TO THE ICOC IN AUGUST WHERE THEY APPROVED THE LANGUAGE WE HAD SUBMITTED.

THAT WENT INTO THE FORMAL OFFICE OF ADMINISTRATIVE LAW REVIEW AND APPROVAL WHERE THEY SORT OF NOW LOOK AT EVERYTHING COLLECTIVELY, THE REGULATIONS, THE COMMENTS, THE RESPONSE TO COMMENTS, EVERYTHING WE HAD DONE, AND THEY HAD AN ADDITIONAL 60 COMMENTS WHICH WE HAD TO ADDRESS. SO THAT WAS ANOTHER ROUND OF CLARIFICATION, CLEANING UP THE RECORD, MAKING EVERYTHING CLEAR FOR THE OFFICE OF ADMINISTRATIVE LAW. AND WE GOT THE LETTER THAT SAID ON THE 10TH OF OCTOBER YOUR REGULATIONS BECOME FORMAL STATE LAW. AND I THINK YOU ALL GOT AN E-MAIL FROM ME WHICH REPRESENTED A COLLECTIVE SIGH OF RELIEF.

IN ADDITION, IN SEPTEMBER WE HAD THE IOM WORKSHOP DEALING WITH OOCYTE DONATION AND STEM CELL RESEARCH. DR. LINDA GUIDICE WILL BE REPORTING ON THOSE FINDINGS TODAY. THAT WILL BE THE MAJOR PORTION OF TODAY'S MEETING.

THIS IS NOW TO KIND OF GET YOU UP TO SPEED ON WHAT WE'VE BEEN UP TO FOR THE LAST FEW MONTHS. A REMINDER, WE HAD A TELECONFERENCE IN OCTOBER, YOU REMEMBER, AND THAT'S WHERE WE DISCUSSED FETAL TISSUE REGULATION. THAT REGULATION IS NEARING THE END OF ITS

LIFE CYCLE AND HOPEFULLY WILL BECOME STATE LAW FAIRLY SOON. THE ICOC IN DECEMBER APPROVED THE LANGUAGE THAT YOU ALL RECOMMENDED.

AND THEN I'D LIKE TO SORT OF DRAW YOUR ATTENTION TO THAT SORT OF LONG BLUE BAR, WHICH IS AT THE END OF LAST YEAR, WE STARTED WHAT'S DESCRIBED AS A CIRM EVALUATION INITIATIVE. IN YOUR PACKET YOU HAVE THE FOUR-PAGE WHITE PAPER. YOU RECEIVED THAT PREVIOUSLY, BUT AN ADDITIONAL COPY IS IN YOUR PACKET.

WHAT THAT INITIATIVE WAS ORIENTED TOWARDS IS GOING OUT TO MEET WITH INSTITUTIONAL REPRESENTATIVES, CHECKING IN, AND REALLY STARTING TO UNDERSTAND, OKAY, WE'VE PUT REGULATIONS OUT THERE. YOU ALL ARE TAKING THEM VERY SERIOUSLY. YOU'RE IN THE MIDST OF DEVELOPING GRANT PROPOSALS. IS THERE ANYTHING HERE THAT'S CLEAR, THAT'S NOT CLEAR? WE'RE TRYING TO REALLY GROUND TRUTH THE WORK WE'VE DONE IN TERMS OF IMPLEMENTATION. HOW'S IT WORKING?

THE SORT OF FOCUS WITH THE INSTITUTIONS WAS A SERIES OF WORKSHOPS, ONE AT STANFORD AND ONE AT THE BURNHAM INSTITUTE ON THE SAN DIEGO PENINSULA. SORT OF MEAT OF THAT EFFORT, THE FINDINGS, THERE'S A REPORT IN YOUR BINDER, BUT THE BIG PART OF MY PRESENTATION TOMORROW WILL REALLY GO INTO MUCH MORE DETAIL IN TERMS OF SOME OF THE LESSONS LEARNED, AND THAT WILL BUILD UP

TO A CONVERSATION OF POLICY ISSUES WE MAY WANT TO CONSIDER IN THE FUTURE. I WOULD LIKE TO CHARACTERIZE IT AT THIS POINT AS WE'VE KIND OF PUT OUT A PRODUCT THAT APPEARS TO BE RATHER EFFECTIVE, BUT WE MIGHT NEED TO DO SOME TINKERING AROUND THE EDGES. SO I WILL PRESENT SOME OF THOSE ISSUES TO YOU.

IN THE MEANTIME THE LITTLE BLUE CIRCLES DOWN THERE, AS BERNIE MENTIONED, WE'VE HAD TWO GRANT REVIEWS AND THE ICOC APPROVED FOR FUNDING -- I BELIEVE THAT'S THE CORRECT NUMBER -- ABOUT 150 MILLION. AM I GETTING THAT NUMBER RIGHT? AND LET'S SEE. THAT BRINGS US UP TO WHERE WE ARE TODAY, OUR ANNUAL MEETING, WHICH A COUPLE OF PEOPLE HAVE QUESTIONED WHY ARE WE CALLING IT THE ANNUAL MEETING? THERE IS ACTUALLY A PROVISION IN PROPOSITION 71 THAT SAYS THIS WORKING GROUP SHALL HAVE AN ANNUAL MEETING. SO THIS IS WHAT WE'RE CALLING IT. THIS IS THE ANNUAL MEETING.

SO JUST TO SUMMARIZE NOW, JUST TO FOCUS ON THE REGULATORY ISSUES, AS I MENTIONED, WE GOT APPROVAL IN OCTOBER. I MISSPOKE. THEY FORMALLY TOOK EFFECT ON THE 22D OF NOVEMBER. THAT WAS THE ENTIRE REGULATORY PACKAGE. THERE WERE A COUPLE OF SECTIONS IN THERE WHICH WE RAN INTO INSURMOUNTABLE OBSTACLES WITH THE OFFICE OF ADMINISTRATIVE LAW. ONE WAS SECTION 1000120 WHICH DEALS WITH RECORDKEEPING. WE'VE SUBSEQUENTLY

REVISED THAT SECTION AND RETURNED IT TO THE OFFICE OF ADMINISTRATIVE LAW. OUR LAST CHECK ON THAT IS IT IS SORT OF JUST SITTING IN THE OFFICE OF ADMINISTRATIVE LAW. SOMETIMES REGULATIONS HAVE A HABIT OF GOING IN, AND YOU KIND OF HAVE TO NUDGE THEM OUT, SO WE'VE SORT OF INITIATED THE NUDGING PROCESS, AND WE'RE HOPING TO HEAR BACK SHORTLY.

THERE WAS ANOTHER SECTION, 100130, THAT WAS THE SECTION, IF YOU WILL REMEMBER, WE ORIGINALLY HAD SOME VERY EXTENSIVE LANGUAGE ABOUT MATERIAL SHARING, MATERIALS DERIVED WITH CIRM FUNDING, HOW THEY SHOULD BE PUT OUT TO OTHER RESEARCHERS. AND THEN AS THAT CONVERSATION MOVED FORWARD, WE THEN INITIATED AT CIRM A PROCESS TO DEVELOP AN IP POLICY OR AN INTELLECTUAL PROPERTY POLICY. THAT WHOLE NEW INITIATIVE TOOK OFF IN THAT AREA. WE'RE GOING TO GET AN UPDATE TOMORROW ON THE IP POLICY. AND AS A RESULT, IT REALLY NULLIFIED THE NEED FOR THIS GROUP TO BE SORT OF DEVELOPING LANGUAGE IN THAT AREA. IT WAS CLEARLY A MUCH BIGGER ISSUE THAN WE COULD DEAL WITH INDEPENDENTLY. SO YOU WILL GET AN UPDATE TOMORROW FROM MARY MAXON ON THAT EFFORT.

AGAIN, THE REVISIONS TO SECTION 100120 APPROVED BY THE ICOC ON THE 12TH OF DECEMBER, AS I MENTIONED, THEY'RE UNDER OAL REVIEW.

FINALLY, THE FETAL TISSUE SECTION, WHICH I MENTIONED EARLIER, THE COMMENT PERIOD CLOSED WITHOUT ANY PUBLIC COMMENT. AND WE SHOULD BE ABLE TO MOVE THAT INTO THE FINAL STAGE OF OAL APPROVAL PENDING APPROVAL BY THE ICOC AT ITS JUNE 4TH MEETING. THE ICOC IS MEETING ON JUNE 4TH AND 5TH NEXT MONTH, AND WE'RE NOW PLANNING ON BRINGING THAT TO THE ICOC ON THE 4TH, NOT THE 5TH.

AS SOME YOU HAVE MET TAMAR. WE NOW HAVE A CHIEF LEGAL COUNSEL. LORI HOFFMAN IS OUR ACTING PRESIDENT, AND I'D LIKE TO INTRODUCE YOU TO LORI. ALSO, OUR ARLENE CHIU IS THE INTERIM CHIEF SCIENTIFIC OFFICER. ARLENE IS NOT WITH US TODAY, BUT THAT COVERS OUR EXECUTIVE STAFF, WHICH YOU'VE NOT MET YET.

AND, AGAIN, THE ICOC MEETS ON JUNE 5TH. AND IN ADDITION TO CONSIDERING OUR FETAL TISSUE REGULATION, WHICH IS PERHAPS THE MOST RIVETING PART OF THE AGENDA, THEY WILL ALSO BE CONSIDERING THE RECOMMENDATIONS OF THE PRESIDENTIAL SEARCH SUBCOMMITTEE, SO THAT GIVES YOU A SENSE OF THE TIMELINE FOR A NEW PRESIDENT.

FINALLY, I'D LIKE TO DRAW YOUR ATTENTION TO SOME MATERIALS THAT WE'VE PUT TOGETHER OR THAT ARE AVAILABLE. YOU SHOULD HAVE RECEIVED A MEMBER MANUAL, WHICH THE MEMBER MANUAL, I DON'T HAVE IT ILLUSTRATED HERE IN THE GRAPHICS, BUT THAT WOULD INCLUDE ALL THE

MATERIALS YOU ALL ARE INTERESTED IN OR MAY REQUIRE AS A WORKING GROUP MEMBER. IT INCLUDES A NUMBER OF THE POLICIES, CONFLICT OF INTEREST, AND THAT SORT OF DOCUMENTATION. IN ADDITION, WE PUT TOGETHER ALL THE INFORMATION, I THINK, THAT'S SORT OF SUBSTANTIVE THAT RELATES TO THE REGULATIONS. I HOPE THAT'S A USEFUL RESOURCE.

IN ADDITION TO THE MANUAL, THERE WAS A CD THAT WENT WITH THAT, AND THE CD INCLUDED ALL THE ADDITIONAL DOCUMENTATION SORT OF SUPPORTING OUR REGULATIONS. IT'S VERY GOOD BEDTIME READING. AGAIN, WE WANTED TO MAKE THAT AVAILABLE TO YOU. IF FOR SOME REASON YOU REQUIRE AN ADDITIONAL COPY OR DID NOT RECEIVE YOUR COPY, WE CAN PROVIDE THAT TO YOU TODAY.

IN ADDITION, YOU HAVE A COPY IN YOUR BINDER OF THE FINAL REPORT FROM THE IOM RELATING TO EGG DONATION. THE CIRM STRATEGIC PLAN WAS INCLUDED IN THE CD WHICH I MENTIONED, AND THE CIRM ANNUAL REPORT IS ALSO INCLUDED. AND WE CAN PROVIDE YOU WITH PRINTED COPIES OF THOSE DOCUMENTS IF YOU REQUIRE THEM AS WELL.

SO WITH THAT SAID, THAT'S MY REPORT FOR NOW. AGAIN, I THINK THE MEAT OF THE STAFF CONTRIBUTION TO THIS MEETING WILL BE TOMORROW WHEN WE SUMMARIZE THE FINDINGS FROM OUR EVALUATION INITIATIVE. AND I'M NOTICING THAT LINDA HASN'T ARRIVED. EXCUSE ME. I

APOLOGIZE.

CHAIRMAN LO: SHE'S READY TO GO. BEFORE WE CALL LINDA, I JUST WANT TO ASK LORI. DO YOU WANT TO SAY ANYTHING TO THE COMMITTEE OR TAMAR, GREETINGS, WHATEVER? GLAD TO HAVE YOU BOTH, AND WE LOOK FORWARD TO WORKING WITH YOU.

SO, GEOFF, MY COPY OF THE -- OUR NEXT ORDER OF BUSINESS IS TO TURN TO THE REPORT, "ASSESSING THE MEDICAL RISKS OF HUMAN OOCYTE DONATION FOR RESEARCH." THIS WAS A WORKSHOP CARRIED OUT UNDER THE AUSPICES OF THE INSTITUTE OF MEDICINE AND THE NATIONAL ACADEMY OF SCIENCES. CIRM ACTUALLY CONTRACTED WITH IOM, NAS TO CARRY OUT THIS REPORT. AND I THINK THE REASON CIRM WANTED TO DO THAT IS TO REALLY HAVE AN OBJECTIVE, BALANCED, AND PEER REVIEWED REPORT SO THAT IT WOULD STAND UP UNDER CLOSE SCRUTINY.

NOW, THIS IS A WORKSHOP WHICH UNDER INSTITUTE OF MEDICINE AND NATIONAL ACADEMY RULES MEANS THAT THERE ARE NO RECOMMENDATIONS, BUT IS A TRANSCRIPT OF THE PRESENTATIONS THAT WERE MADE IN A PUBLIC MEETING AND INCORPORATES BOTH THE PRESENTATIONS AND THE EXTENSIVE DISCUSSION AT THAT MEETING.

THE CHAIR OF THIS WORKSHOP COMMITTEE WAS DR. LINDA GUIDICE FROM UCSF WHERE SHE'S THE CHAIRPERSON OF THE DEPARTMENT OF OBSTETRICS, GYNECOLOGY, AND

REPRODUCTIVE SCIENCES. AND SHE ALSO HOLDS THE ROBERT JAFFE CHAIR IN REPRODUCTIVE SCIENCES. AND SHE IS A REPRODUCTIVE ENDOCRINOLOGIST WHO CARRIES OUT AN ACTIVE RESEARCH PROGRAM ON TOP OF HER ADMINISTRATIVE DUTIES. AND SHE AND HER COMMITTEE, I THINK, PUT TOGETHER AN EXCELLENT MEETING AND HAVE PREPARED A REPORT, WHICH SHE WILL NOW GIVE US THE HIGHLIGHTS OF. AND WE WILL BE DRAWING HEAVILY ON THIS REPORT FOR ANOTHER ACTIVITY THAT WE WOULD LIKE THE WORKING GROUP TO HELP PLAN.

SO, LINDA, IT'S A PLEASURE FOR US FOR YOU TO BE HERE. AND ONCE AGAIN, WE THANK YOU, AS THE ENTIRE FIELD, FOR THE REPORT WHICH IS VERY INFORMATIVE AND VERY CLEAR AND I THINK VERY USEFUL.

DR. GUIDICE: THANK YOU, BERNIE. IT'S A PLEASURE TO BE HERE TODAY. I AM GOING TO GO THROUGH GIVING AN OVERVIEW OF A BACKGROUND OF SOME OF THE PROCEDURES THAT SUBJECTS WHO ARE DONATING OOCYTES FOR RESEARCH --

DR. PRIETO: COULD THE SPEAKER BE CLOSER TO THE MICROPHONE AGAIN, PLEASE?

DR. GUIDICE: SURE. IS THAT BETTER? OKAY. I'M GOING TO GIVE AN OVERVIEW OF SOME OF THE PROCEDURES THAT SUBJECTS UNDERGO AND ALSO WOMEN UNDERGO FOR FERTILITY THERAPY WITH REGARD TO RETRIEVING EGGS.

SO AS BERNIE HAS MENTIONED, WE WERE ASKED TO

PUT TOGETHER A COMMITTEE AND ALSO -- I'M SORRY -- A WORKSHOP AND A REPORT. AND THE COMMITTEE MEMBERS WERE CHOSEN BY PRIMARILY THE INSTITUTE OF MEDICINE AND THE NATIONAL RESEARCH COUNCIL AND THEIR ADVISORS. AND AS I'M SURE YOU KNOW, THE IOM IS AN ORGANIZATION WHOSE MISSION IS TO ADVISE THE NATION AND IMPROVE HEALTH.

THE ROSTER, COMMITTEE ROSTER, LIST MEMBERS HERE. SOMEONE HAS FALLEN OFF THIS. THAT'S DR. MARCELLE CEDARS FROM UCSF, SO SHE SHOULD BE RIGHT ABOVE DR. DAVIDSON. SO THERE'S MYSELF AS CHAIR AS A REPRODUCTIVE ENDOCRINOLOGIST; DR. MARCELLE CEDARS, WHO IS THE DIVISION CHIEF OF REI, REPRODUCTIVE ENDOCRINE AND INFERTILITY, AT UCSF. DR. DAVIDSON, EZRA DAVIDSON, WHO IS A GENERALIST OB-GYN AND A LONGTIME MEMBER OF THE INSTITUTE OF MEDICINE, AND HAS SAT ON MANY COMMITTEES AND IS VERY FAMILIAR WITH COMMITTEE PROCESS. NAIHUA DUAN IS A BIOSTATISTICIAN. BERNIE HARLOW IS AN EPIDEMIOLOGIST. SUSAN KLOCK, A PSYCHOLOGIST WHO HAS WORKED PRIMARILY WITH EGG DONORS. JUDITH LA ROSA, HER EXPERTISE IS IN WOMEN'S HEALTH BROADLY SPEAKING. SHE'S A PHYSICIAN. CATHERINE RACOWSKY IS AN EMBRYOLOGIST WORKING WITH HUMAN EGGS AND SPERM AND EMBRYOS. ZEV ROSENWAKS IS A REPRODUCTIVE ENDOCRINOLOGIST WORKING AT CORNELL. AND JOE LEIGH SIMPSON IS ALSO A REPRODUCTIVE ENDOCRINOLOGIST AND A GENETICIST AND ALSO A MEMBER OF

THE IOM AS IS ZEV ROSENWAKS.

THE STATEMENT OF OUR TASK WAS TO EXPLORE AND ASSESS THE NATURE AND MAGNITUDE OF THE POTENTIAL MEDICAL RISKS ASSOCIATED WITH OOCYTE DONATION FOR STEM CELL RESEARCH WITH AN EYE TOWARDS IDENTIFYING WHAT WE KNOW, WHAT WE NEED TO KNOW, AND WHAT STRATEGIES MIGHT BE EMPLOYED TO REDUCE THE POTENTIAL RISKS ASSOCIATED WITH THIS PROCEDURE.

WE HAD A VERY TIGHT TIMELINE. THE PROJECT START-UP WAS IN JUNE OF 2006. OUR FIRST MEETING WAS JUST WITHIN THREE TO FOUR WEEKS IN JULY. AT THIS MEETING ALL OF THE MEMBERS ASSEMBLED ALONG WITH NAS STAFF AND WE PLANNED OUT WHAT WERE THE ISSUES. AND WE DISCUSSED THIS, AND THEN WE ALSO PUT TOGETHER A ROSTER OF INDIVIDUALS TO INVITE. WE PUT TOGETHER THE AGENDA FOR THE WORKSHOP AND ALSO WHOM TO INVITE TO THE WORKSHOP. WE HAD A MEETING JUST A COUPLE OF DAYS BEFORE THE WORKSHOP TO BE SURE EVERYTHING WAS ON TRACK, NUMEROUS E-MAILS AND TELECONFERENCES IN BETWEEN, AND THEN THE WORKSHOP HELD ON SEPTEMBER 28TH AT THE HYATT, I BELIEVE, OR THE HILTON AT THE AIRPORT.

WE HAD A WRITER, A SCIENCE WRITER, AND NUMEROUS DRAFTS OF OUR REPORT, WHICH IS PURELY A SUMMARY OF THE EVENTS THAT WERE DISCUSSED AT THE MEETING. SO THERE'S NO EDITORIALIZING, THERE'S NO

ADDITIONAL INFORMATION. ACCURACY OF INFORMATION WAS CERTAINLY CHECKED. AND AS BERNIE SAID, OUR CHARGE WAS NOT TO MAKE RECOMMENDATIONS, BUT RATHER TO ESSENTIALLY DESCRIBE THE STATE OF THE SCIENCE AND THE STATE OF THE MEDICINE. AND THE REPORT WAS RELEASED EARLIER THIS YEAR IN JANUARY.

SO THE GOALS OF TODAY ARE TO GO THROUGH THE PROCESS TO PROCURE HUMAN OOCYTES. WHAT IS THE MAGNITUDE OF THE RESOURCE, WHICH CERTAINLY IMPACTS ON THE AVAILABILITY OF SUBSTRATE FOR EXPERIMENTS? WHAT ARE THE RISKS INVOLVED? HOW GOOD ARE THE DATA IN TERMS OF THOSE RISKS? AND WHAT ARE SOME OF THE SOLUTIONS?

I'M SURE YOU ALL KNOW THAT THERE'S NATURAL REPRODUCTION AND THERE'S ALSO IN VITRO FERTILIZATION. AND IN IVF FOR THERAPY FOR INFERTILITY, GAMETES, THAT IS, EGGS AND SPERM, ARE OBTAINED FROM PATIENTS OR DONORS, PERHAPS A SPERM DONOR OR AN EGG DONOR OR SOMETIMES BOTH. EMBRYOS ARE THEN CREATED, AND THESE ARE USUALLY TRANSFERRED FOR THERAPY. FOR HUMAN EMBRYONIC STEM CELL RESEARCH, IT IS THE EMBRYO AT THE BLASTOCYST STAGE THAT IS USED FOR THE INNER CELL MASS TO GENERATE CELL LINES. AND GAMETES, IN PARTICULAR EGGS, ARE THE TOPIC FOR USE IN SOMATIC CELL NUCLEAR TRANSFER WHERE AN EGG WILL HAVE ITS NUCLEUS TAKEN OUT, THE NUCLEUS THEN OF A SOMATIC CELL, I.E., NOT AN EGG

CELL, NOT A SPERM CELL, IS PUT IN. AND THEN THIS REPROGRAMS AND YOU END UP GENERATING EMBRYOID OR EMBRYO-LIKE STRUCTURE THAT HAS AN INNER CELL MASS, AND CELLS CAN THEN BE OBTAINED FOR THAT.

THE ASSISTED REPRODUCTIVE TECHNOLOGIES GO BACK A VERY LONG WAY. THE FIRST BABY WAS BORN IN 1984 IN THIS COUNTRY AND 1978 IN THE UNITED KINGDOM. IT'S A COLLECTION OF THERAPIES TO ACHIEVE A PREGNANCY INVOLVING PATIENTS, SPERM DONORS, EGG DONORS, SOMETIMES SURROGATES. AND THE OLD PARADIGM WAS SOME DONATION OF EMBRYOS AND EGGS FOR THE USE OF OTHER INDIVIDUALS USUALLY FOR REPRODUCTIVE PURPOSES AND SOMETIMES FOR RESEARCH. THIS SET OF --

(DISCUSSION OFF THE RECORD REGARDING THE TRANSMISSION.)

DR. GUIDICE: IN ADDITION TO FERTILITY THERAPY, THE ASSISTED REPRODUCTIVE TECHNOLOGIES HAVE NOW GIVEN AN OPPORTUNITY FOR SUBJECTS AND PATIENTS, EITHER PATIENTS WHO BECOME SUBJECTS OR SUBJECTS WHO ARE NOT UNDERGOING THERAPY, TO PARTICIPATE IN HUMAN EMBRYONIC STEM CELL AND SOMATIC CELL NUCLEAR TRANSFER RESEARCH WITH THE HOPE OF THE PROMISE OF CURES FOR CHRONIC DISEASES.

THERE'S A NEW PARADIGM THAT HAS BEEN INTRODUCED. AND THAT IS FOR INDIVIDUALS OR COUPLES

UNDERGOING ASSISTED REPRODUCTION PROCEDURES SOLELY TO DONATE GAMETES OR EMBRYOS FOR RESEARCH. SO THAT IS NOT IN COMMON PRACTICE IN THIS COUNTRY. BUT SOME OF THE MOTIVATING FACTORS MAY BE FOR EVENTUAL HELP OF FAMILY MEMBERS WHO MAY BE AFFECTED BY A GENETIC DISORDER OR A CHRONIC DISEASE FOR MONEY OR ALTRUISTICALLY.

IN 2004 WHERE THE DATA WERE REPORTED IN DECEMBER OF 2006, THERE WERE ABOUT 123,000 ASSISTED REPRODUCTIVE TECHNOLOGY CYCLES IN THE UNITED STATES, AND THERE ARE 437 CLINICS PERFORMING MOST OF THESE CYCLES. THERE WERE 35,786 LIVE BIRTHS. AND OF THOSE CYCLES IN WHICH FRESH EMBRYOS WERE TRANSFERRED, 74 PERCENT OF THESE CYCLES WERE WITH FRESH EMBRYOS AND NOT USING A DONOR EGG. 14 PERCENT USED FROZEN EMBRYOS, BUT NOT WITH A DONOR EGG USED. AND 8 PERCENT WERE FRESH CYCLES WHERE A DONOR EGG WAS USED IN THE ATTEMPT TO CONCEIVE, AND 3.4 PERCENT USED FROZEN EMBRYOS WHERE A DONOR EGG WAS USED AS AN ATTEMPT TO CONCEIVE. SO ABOUT 11 PERCENT OF THESE CYCLES, SO ABOUT 13,000 ART CYCLES, ARE DONOR EGG CYCLES FOR THE PURPOSE OF FERTILITY AND PREGNANCY.

YOU CAN SEE THAT ABOUT 11,000 CYCLES WERE DISCONTINUED BEFORE THE EGG RETRIEVAL PRIMARILY FOR POOR EGG PRODUCTION, BUT THERE WERE ALSO SOME CANCELLATIONS FOR MEDICAL COMPLICATIONS. THESE DATA

ARE FROM THE SART, SOCIETY FOR ASSISTED REPRODUCTIVE TECHNOLOGIES, WHICH IS A MEMBER OF THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE.

SO IN THE PROCUREMENT PROCESS, WHEN A COUPLE COMES IN OR AN INDIVIDUAL COMES IN, THERE'S A HISTORY AND PHYSICAL EXAM, A REVIEW, AN EXTENSIVE REVIEW OF FAMILY HISTORY, AND PSYCHOLOGICAL SCREENING. AND THERE IS INFORMED CONSENT WITH REGARD TO THE PROCEDURES, THE MEDICATIONS, THE RISKS, AND THE BENEFITS, AND THE ALTERNATIVES. ALSO, A RATHER ELABORATE PART OF THIS INFORMED CONSENT IS THE DISPOSITION OF THE EMBRYOS AND THE GAMETES. PRIOR TO HUMAN EMBRYONIC STEM CELL RESEARCH AND SOMATIC CELL NUCLEAR TRANSFER, THE DISPOSITION OF THE EMBRYOS WAS PRIMARILY EITHER FOR CRYOPRESERVATION AND FOR LATER USE OR FOR DONATING TO RESEARCH, AND THE THIRD OPTION WAS TO DISCARD UNWANTED OR UNUSED EMBRYOS OR GAMETES.

THE FEMALE PARTNER UNDERGOES A SIGNIFICANT AMOUNT OF HORMONAL TESTING AND ANATOMIC TESTING FOR FERTILITY PURPOSES. AND THE MALE IS EVALUATED BY A SEMEN ANALYSIS INITIALLY. IN ADDITION, ALL SUBJECTS IN THE STATE OF CALIFORNIA, CURRENTLY ALL SUBJECTS UNDERGOING EITHER ASSISTED REPRODUCTION OR ARTIFICIAL INSEMINATION OR PARTNER INSEMINATION UNDERGO INFECTIOUS DISEASE TESTING, INCLUDING HIV, HUMAN TUMOR LEUKEMIA

VIRUS 1 AND 2, HDLV I AND II, HEPATIS B AND C, AND A SYPHILIS TEST.

SO THE PROCUREMENT PROCESS CONSISTS OF SUBJECTS OR PATIENTS WHO UNDERGO, FIRST, AN INITIAL CONSULTATION, TESTING, CONSENTING, AND THEN INJECTION TEACHING. AND THE REASON FOR INJECTION TEACHING IS THAT IN ORDER TO -- THE GOAL HERE IS TO GET MANY EGGS. NORMALLY IN AN OVARY ONLY ONE EGG DEVELOPS PER CYCLE. ONLY ONE EGG OVULATES PER CYCLE; SEVERAL DEVELOP, AND THIS IS AN IMPORTANT POINT. A WHOLE GROUP WILL BE COMMITTED TO DEVELOPMENT FOR THAT CYCLE, BUT ONLY ONE MAKES IT AND ALL THE OTHERS DIE OFF. WHAT THIS PROCESS DOES IS IT USES INJECTABLE FSH, FOLLICLE STIMULATING HORMONE, AND A LITTLE BIT OF LH, TO SAVE THOSE THAT WERE DESTINED TO DIE OFF AND BE PART OF THIS GROUP OR THIS COHORT THAT GETS DEVELOPED FOR THAT CYCLE. SO THIS CAN BE ANYWHERE FROM ONE MORE FOLLICLE OR EGG FOR A CYCLE, OR IT COULD BE 25 MORE FOLLICLES DEPENDING ON A NUMBER OF THINGS, AS WE'LL GET INTO SHORTLY, AND THIS IS ACTUALLY THE BASIS OF SOME OF THE RISK THAT'S INVOLVED IN THE MEDICAL THERAPY.

SO SUBJECTS AND PATIENTS SELF-INJECT BY SUBCUTANEOUS INJECTION FSH AND LH. IN ADDITION, THEY USUALLY TAKE ANOTHER MEDICATION CALLED THE GNRH AGONIST, WHICH IS BASICALLY TO PREVENT THEM FROM HAVING

AN LH SURGE AND, THEREFORE, PREVENTING THEM FROM OVULATING BECAUSE THE TEAM NEEDS TO GET IN THERE TO GET THE EGGS OUT BEFORE THEY ALL OVULATE. AND WHEN EVERYTHING LOOKS GOOD, I.E., WHEN THE FOLLICLES DEVELOP TO A CERTAIN SIZE AND THE ESTRADIOL LEVEL IS AT A CERTAIN LEVEL AND IS RISING, THEN HCG IS GIVEN. THIS IS ANOTHER HORMONE THAT'S GIVEN BY INJECTION TO MAKE THE EGGS DEVELOP AND MATURE. AND WITHIN 36 TO 41 HOURS LATER, USUALLY THE EGGS ARE READY TO POP OUT OR OVULATE, AND THAT'S WHEN THE EGG RETRIEVAL IS DONE, SO THE TAKING OUT OF THE EGGS, AS YOU WILL SEE SHORTLY.

SO THIS IS THE PROCESS THAT AN EGG DONOR WOULD UNDERGO, AND IT'S THE SAME PROCESS THAT A PATIENT UNDERGOING FERTILITY THERAPY WOULD UNDERGO. THE REST OF THE PROCESS IN TERMS OF INSEMINATING THESE RETRIEVED EGGS, WATCHING THE EMBRYOS DEVELOP, AND THEN TRANSFERRING IS VERY SPECIFIC TO PATIENTS WANTING FERTILITY THERAPY, BUT THERE MAY BE SUBJECTS WHO WOULD WANT TO HAVE EMBRYOS CREATED AND HAVE THE INNER CELL MASS THEN GIVE RISE TO HUMAN EMBRYONIC STEM CELL LINES.

SO HOW DO WE GET THE EGGS OUT? THE PATIENTS ARE USUALLY OR SUBJECTS ARE USUALLY IN A SPECIAL PROCEDURE ROOM. THERE'S USUALLY AN ANESTHESIOLOGIST PRESENT. AND THE PROCEDURE IS FORMED UNDER LIGHT ANESTHESIA, PRIMARILY CONSCIOUS SEDATION. SO THIS IS

NOT AN INTUBATION. THERE'S NOT A TUBE DOWN THE THROAT. IT'S NOT DEEP ANESTHESIA. IT'S LIGHT ANESTHESIA. EVERYTHING IS DONE UNDER STERILE CONDITIONS. AND THEN A TRANSVAGINAL ULTRASOUND PROBE IS PLACED. AND I SHOULD MENTION HERE WHILE INJECTIONS ARE BEING MADE, USUALLY ON A DAILY BASIS, THE PATIENT USUALLY COMES IN EVERY FEW DAYS FOR AN ULTRASOUND TO LOOK AT HOW THE FOLLICLES ARE DEVELOPING, AND SHE OFTEN WILL GET A BLOOD TEST FOR ESTROGEN OR ESTRADIOL.

SO THIS IS THE ULTRASOUND PROBE. IT'S TRANSVAGINAL. THERE'S A STERILE COVER ON IT, AND THIS LONG SKINNY THING IS THE ASPIRATING NEEDLE THAT'S ATTACHED WITH SOME TUBING TO A TEST TUBE. AND THERE'S A SUCTION AS WELL. SO WHEN THE PROBE IS PLACED INTO THE VAGINA, IT'S PUT INTO THE BACK OF THE VAGINA, AND THEN UNDER ULTRASOUND GUIDANCE -- MY POINTER IS BECOMING ANEMIC HERE. IN THE UPPER RIGHT YOU CAN SEE THAT BLACK CIRCLES ARE THE FOLLICLES, AND RIGHT THERE IS THE ASPIRATING NEEDLE. AND SO THAT'S WHAT THE OPERATOR USES AS A GUIDE TO GET THE EGGS OUT. NOW, A LOT OF THINGS LOOK BLACK AND ROUND IN THE PELVIS. THERE COULD BE BLOOD VESSELS. THERE COULD BE FLUID IN THE GUT. HOWEVER, USUALLY DURING THE MONITORING PROCESS, THE OPERATOR OR THE SKILLED ULTRASONOGRAPHER IS AWARE OF WHERE THESE STRUCTURES ARE AND HOW MANY ARE

THERE AND ARE THEY GROWING, AND USUALLY BLOOD VESSELS DON'T GROW OVER A TWO-WEEK OR A WEEK PERIOD.

SO WHEN THE NEEDLE IS PUT IN, THEN THE SUCTION IS APPLIED, THE FOLLICLE COLLAPSES, THE EGG USUALLY COMES OUT, AND IT FINDS ITS WAY INTO THAT TEST TUBE RIGHT THERE. THAT'S GIVEN TO AN EMBRYOLOGIST WHO THEN LOOKS TO SEE IF THE EGG IS THERE AMONG A LOT OF OTHER CELLS. SO ONCE EGGS ARE RETRIEVED, THEN THERE'S AN OPPORTUNITY POTENTIALLY TO DO SOMATIC CELL NUCLEAR TRANSFER. MORE COMMONLY, THE EGGS ARE INSEMINATED. AND THEN AFTER INCUBATION, THEY'RE USUALLY TRANSFERRED INTO THE UTERINE CAVITY IN THE RIGHT LOWER CIRCLE. AND THAT'S THE TRANSFER CATHETER, THAT LITTLE WHITE THING. AND THE LITTLE EMBRYOS ARE SQUIRTED UP HERE. FOR HUMAN EMBRYONIC STEM CELL LINE DERIVATION, THE EMBRYOS, RATHER THAN BEING TRANSFERRED, WOULD BE OBTAINED AND EITHER GROWN TO THE FIVE-DAY STAGE, WHICH IS THE BLASTOCYST STAGE, AND THE INNER CELL MASS THEN OBTAINED FOR LINE DERIVATION.

FOR EGG DONORS, COMMONLY THE DONOR IS GIVEN THE EXACT SAME TYPE OF STIMULATION. THE EGGS ARE HARVESTED, AND THERE IS A PROCESS CALLED NOW EGG SPLITTING THAT IS SOMETIMES PURSUED IN IVF CLINICS WHERE A WOMAN CAN HAVE A DISCOUNT ON HER IVF CYCLE IF SHE SHARES HER EGGS WITH ANOTHER WOMAN. THERE IS SOME

DISCUSSION ALSO WITH REGARD TO EGG SPLITTING FOR GIVING EGGS FOR RESEARCH. AND SO HERE ABOUT 14,000 DONOR EGG CYCLES. YOU CAN SEE THE MAGNITUDE OF THE NUMBER OF CYCLES.

SO WHAT ARE THE RISKS? AFTER GOING THROUGH ALL OF THAT PROCEDURE, THERE ARE SEVERAL RISKS THAT FALL INTO TWO TYPES OF CATEGORIES. AND THIS IS WHAT WE DISCUSSED AT THE COMMITTEE AND AT THE WORKSHOP. THE ACUTE RISKS, THE FIRST ONE BEING OVARIAN HYPERSTIMULATION SYNDROME. SO YOU CAN IMAGINE AS THE OVARIES ARE GROWING, THERE MAY BE SOME EFFECTS IN TERMS OF THE OVARIES GETTING LARGER, AND THERE ARE RISKS ASSOCIATED WITH THAT, AS WE'LL GET INTO. THERE ARE ALSO SURGICAL RISKS, POTENTIALLY ANESTHETIC RISKS, POTENTIALLY PSYCHOLOGIC RISKS, AND THERE MAY BE DIFFERENCES BETWEEN PSYCHOLOGIC RISKS BETWEEN EGG DONORS FOR RESEARCH AND EGG DONORS FOR FERTILITY AND PREGNANCY.

THEN THERE ARE THE ISSUES OF POTENTIAL CHRONIC RISKS WITH REGARD TO STEROID HORMONE OR ESTROGEN-DEPENDENT CANCERS BECAUSE THE ESTROGEN LEVELS IN THESE CYCLES TEND TO GET SOMETIMES TENFOLD ABOVE NORMAL FOR A BRIEF PERIOD OF TIME, BUT STILL THERE'S EXPOSURE. AND THEN THE ISSUE OF POTENTIALLY FUTURE FERTILITY.

SO OVARIAN HYPERSTIMULATION SYNDROME, DR. CEDARS GAVE A VERY THOROUGH PRESENTATION AND A REVIEW OF THE LITERATURE. AND WHAT THIS IS IS AN EXAGGERATION OF A DESIRED RESPONSE. IT'S MARKED BY AN INCREASED SIZE OF THE OVARIES, SOMETIMES WITH UPSET STOMACH OR OTHER GASTROINTESTINAL SYMPTOMS. AND THE LAST BULLET POINT IS THE ONE THAT IS PERHAPS THE MOST CONCERNING, AND THAT IS INCREASED VASCULAR PERMEABILITY. DEPENDING ON THE STAGE, AND WE'LL GO THROUGH THE STAGING, THERE CAN BE AN ACCUMULATION OF INTRAABDOMINAL FLUID, DECREASED INTRAVASCULAR VOLUMES. SO THE FLUID FROM THE BLOOD VESSELS CAN GO INTO THE ABDOMEN. THAT RESULTS IN HEMOCONCENTRATION, CONCENTRATION OF THE BLOOD CELLS IN THE CIRCULATION. IT CAN ALSO RESULT IN DECREASED BLOOD FLOW TO THE KIDNEYS AND ALSO CAN BE ASSOCIATED WITH ACTIVATION OF VASO CONSTRICTOR AND ANTI-NATIURETIC FACTORS, SO CLOSING DOWN OF SOME VESSELS AND PREVENTING NATIURESIS.

SO OVARIAN HYPERSTIMULATION SYNDROME, AGAIN, ENLARGEMENT OF THE OVARIES DUE TO OVARIAN STIMULATION WITH GONADOTROPINS. AND THE SECOND PART OF THE PHRASE, AND ADMINISTRATION OF HCG IS A VERY IMPORTANT PART OF THIS ASSESSMENT. AND THAT IS BECAUSE RARELY, RARELY DO WE GET OVARIAN HYPERSTIMULATION SYNDROME IN THE ABSENCE OF GIVING THE TRIGGER FOR EGG MATURATION AND OVULATION.

SO THIS IS ONE TYPE OF CLASSIFICATION THAT WE DISCUSSED. THERE'S MINIMUM OHSS. MOST WOMEN UNDERGOING OVARIAN STIMULATION HAVE SOME DEGREE OF ENLARGED OVARIES AND SOME LOWER ABDOMINAL DISCOMFORT. IT'S USUALLY REVERSIBLE AND DOES NOT REQUIRE MEDICATION, ANALGESICS, OR HOSPITALIZATION.

MODERATE OHSS IS CHARACTERIZED BY ABDOMINAL DISCOMFORT AND FLUID ACCUMULATION OR ABDOMINAL ASCITES, NAUSEA AND VOMITING, AND A NORMAL HEMATOLOGIC PROFILE. SO WITHOUT THE CONCENTRATION OF THE BLOODS CELLS.

AND THEN SEVERE OHSS, WHICH OCCURS, AND SOME OF THESE NUMBERS ARE REALLY DIFFICULT TO PINPOINT, BUT THE GOING ESTIMATE IS ABOUT 0.1 TO 0.2 PERCENT OF WOMEN UNDERGOING THIS PROCEDURE HAVE SEVERE OHSS. AND THERE ARE THREE TYPES OF GRADES. GRADE A IS OUTPATIENT TREATMENT, AND THESE ARE FOR PATIENTS OR SUBJECTS WHO HAVE DYSPNEA OR DIFFICULTY BREATHING BECAUSE OF FLUID THAT'S PUSHING UP UNDER THE DIAPHRAGM, NAUSEA, VOMITING, ENLARGED OVARIES, MARKED ASCITES, MARKED FLUID ACCUMULATION, BUT A NORMAL BIOCHEMICAL PROFILE.

DR. PRIETO: I'M NOT REALLY HEARING YOU.

DR. GUIDICE: I'M LOOKING AT THE SCREEN. IN ADDITION -- SO WE'RE ON THE SLIDE OF OVARIAN HYPERSTIMULATION SYNDROME WITH THE THREE DIFFERENT CLASSIFICATIONS.

AND SO WITH A NORMAL BIOCHEMICAL PROFILE, SO THEIR KIDNEY FUNCTION LOOKS NORMAL, THEIR COAGULATION PROFILE IS NORMAL, AND THEIR LIVER FUNCTIONS ARE NORMAL.

GRADE B IS THE HOSPITAL ADMISSION, WHICH IS CHARACTERIZED BY SEVERE OLIGURIA, OR DECREASED PRODUCTION OF URINE, HEMOCONCENTRATION, ELEVATED CREATININE, WHICH IS A REFLECTION OF KIDNEY FUNCTION, AND ABNORMAL LIVER FUNCTION TESTS, AND THAT REQUIRES HOSPITAL ADMISSION.

THE MOST SERIOUS IS GRADE C IN WHICH THERE IS A RISK OF OR PRESENT THROMBOEMBOLIC EVENTS, AGAIN, WHICH HAS A RANGE OF RISK, 0.7 PER 1,000,000 TO 2.4 PER 10,000. AND THE DATA INCLUDE PREGNANT WOMEN WHO ARE AT THE HIGHEST RISK. AND THE SAME THING IS TRUE WITH RENAL FAILURE. THIS IS A VERY IMPORTANT POINT BECAUSE SUBJECTS WHO ARE DONATING THEIR OOCYTES FOR RESEARCH PRESUMABLY WOULD NOT BECOME PREGNANT. OBVIOUSLY WE WOULDN'T WANT PATIENTS TO HAVE ANY OVARIAN HYPERSTIMULATION, BUT THE MOST SEVERE FORM WITH THE GREATEST COMPLICATION IS IN WOMEN WHO BECOME PREGNANT. AND THAT'S AN ISSUE ALSO WITH REGARD TO HUMAN SUBJECT PROTECTION IN TERMS OF COUNSELING PATIENTS OR SUBJECTS WITH REGARD TO THEIR CHANCE OF BECOMING PREGNANT BECAUSE THERE COULD BE ONE LITTLE EGG THAT WAS JUST NOT

RETRIEVED. AND IF THEY HAVE INTERCOURSE, THEY COULD END UP PREGNANT.

THERE'S AN ADDITIONAL CLASSIFICATION OF OHSS, AND THAT IS EITHER EARLY OR LATE. THE EARLY OCCURS TWO TO SEVEN DAYS AFTER GETTING THE TRIGGER OF HCG, AND THIS IS THE ONE THAT IS MORE APPLICABLE TO THE EGG DONATION POPULATION. THE LATE OHSS OCCURS 12 TO 17 DAYS AFTER HCG. SO IF YOU DO THE MATH, IF A WOMAN IS NOT PREGNANT, SHE'S USUALLY HAD A PERIOD BY THAT TIME, AND THE RISK OF OHSS IS QUITE LOW. HOWEVER, IF SHE IS PREGNANT, AND THIS WE'RE ASSUMING IS NOT THE OVUM DONATION POPULATION, THAT HAS A 4- TO 12-FOLD HIGHER PREVALENCE THAN THE EARLY FORM.

SO YOU CAN SEE THAT MOST OF SEVERE OHSS AND MOST OF LATE OHSS OCCURS IN THE PREGNANT POPULATION FROM THE FERTILITY TREATMENT AS OPPOSED TO THE POTENTIAL EGG DONOR OR THE EGG DONOR POPULATION FOR FERTILITY.

WITH REGARD TO SURGICAL RISKS, THERE CAN BE DAMAGE TO INTERNAL ORGANS DUE TO THE EGG RETRIEVAL PROCEDURE. AS YOU SAW, THE NEEDLE GOES IN UNDER ULTRASOUND GUIDANCE, BUT SOME STRUCTURES LOOK LIKE OTHERS. AND THAT'S ABOUT 0.1 PERCENT RISK. AND THESE DATA WERE SUMMARIZED BY DR. ANA MURPHY OF EMORY UNIVERSITY.

THERE'S ALSO SEVERE -- A SURGICAL RISK IS SEVERE INTRAABDOMINAL BLEEDING, INFECTION. AND IT'S INTERESTING THAT IN 1993, WHEN ONE REPORT WAS PUBLISHED, THE PREVALENCE RATE WAS NINE OUT OF A THOUSAND. AND THEN AFTER AN ASEPTIC TECHNIQUE WAS INTRODUCED, ANOTHER REPORT CAME OUT WITH NO INFECTIONS IN 5,000 EGG RETRIEVALS. TORSION OR TWISTING OF THE OVARY. IF THE OVARY IS BIG AND IT'S ON A LITTLE PEDACLE, IT CAN TWIST ON ITSELF. AND THAT RISK IS ABOUT .13 PERCENT, AND THAT'S A LATE COMPLICATION.

SURGICAL RISKS, INCREASE IN WOMEN WITH PREVIOUS ABDOMINAL SURGERY, KNOWN PELVIC ADHESIONS OR UNKNOWN PELVIC ADHESIONS, AND PREVIOUS PELVIC INFLAMMATORY DISEASE.

DR. LAWRENCE TSEN FROM HARVARD, AN ANESTHESIOLOGIST, REVIEWED THE ANESTHETIC RISKS, AND HE HAS PUBLISHED EXTENSIVELY ON THIS, ESPECIALLY WITH REGARD TO THE IVF POPULATION, WHICH IS WHY WE INVITED HIM TO REVIEW THE LITERATURE AS WELL AS HIS OWN EXPERIENCE.

IV ANESTHESIA, CONSCIOUS SEDATION PRIMARILY, WHICH IS THE WAY ANESTHESIA IS PRIMARILY ADMINISTERED TO WOMEN UNDERGOING THESE PROCEDURES. THE ANESTHETIC RISK INCREASES WITH INCREASING AMERICAN SOCIETY OF ANESTHESIOLOGY SCORES AND ARE HIGHEST IN MEN. SO THIS

IS NOT RELEVANT TO THE DONOR POPULATION.
CO-MORBIDITIES, SO OTHER MEDICAL CONDITIONS THAT ARE ASSOCIATED WITH -- HAVING OTHER MEDICAL CONDITIONS. ELDERLY, WHICH WOULD NOT BE FOR THIS POPULATION. OBESITY, WHICH COULD BE POSSIBLE IN POTENTIAL OOCYTE DONORS. IN-PATIENT, THE PROCESS IS PRIMARILY AN OUTPATIENT PROCEDURE, AND SO NOT CONTRIBUTING TO INCREASED RISK. AND EGG RETRIEVALS ARE NOT EMERGENCIES, AND SO THIS DOES NOT CONTRIBUTE TO THE OVERALL RISK.

THERE ARE MINOR AND MAJOR MORBIDITIES, ESPECIALLY AN INCREASED RISK WITH INCREASING BMI. AND SO THIS GIVES US SOME CLUES IN TERMS OF EVENTUALLY, ALTHOUGH WE HAVEN'T MADE ANY RECOMMENDATIONS, THERE MAY BE INDICATIONS FOR RECOMMENDATIONS FOR EGG DONATION, AND SO BMI MAY BE ON THE TABLE. AND DEATH IS AN EXTREMELY RARE EVENT, AN ANESTHETIC DEATH DURING THIS PROCEDURE. AND BY COMPARISON, IT'S ONE IN 300,000, WHICH IS LESS THAN DRIVING IN YOUR CAR, WHICH IS SOMETHING LIKE ONE IN 50,000.

PSYCHOLOGICAL RISKS, DR. SUSAN KLOCK FROM NORTHWESTERN, A PSYCHOLOGIST, WHO WORKS WITH EGG DONORS PRIMARILY, PRESENTED THESE DATA. AND THERE ARE VERY FEW DATA OUT THERE, AND ALL OF THE DATA ARE ON EGG DONATION FOR FERTILITY. THERE ARE NO DATA ON EGG

DONATION FOR RESEARCH. SO SUBJECTS REPORT MOOD SWINGS LIKELY DUE TO THE FLUCTUATING HORMONES, ANXIETY, REGRET, SOMETIMES FEELING LIKE A COMMODITY, TRAVEL, AND PAIN, PERIODS OF VULNERABILITY DURING SCREENINGS. SO IF YOU ARE PUTTING YOURSELF OUT THERE AS A POTENTIAL EGG DONOR, AND YOU'RE TOLD THAT YOU HAVE POTENTIALLY A DISORDER OR SOMETHING THAT WOULD DISQUALIFY YOU FROM BEING AND EGG DONOR FOR FERTILITY THERAPY, THAT CERTAINLY PUTS YOU IN A VERY VULNERABLE POSITION. ANOTHER VULNERABLE POSITION IS DURING THE DONATION PROCEDURE, THE COUPLE WHO IS WANTING THE EGGS IS VERY AWARE OF HOW THE OVARIES STIMULATE. ARE THEY STIMULATING ON TIME? ARE WE GETTING ENOUGH EGGS? AND MANY OF THE EGG DONORS FEEL PRESSURE. AND THEN POSTDONATION, ONCE THE DONATION IS DONE, THAT'S USUALLY THE END OF THE INVOLVEMENT OF THE EGG DONOR WITH THE FERTILITY PROCESS. AND MANY WOMEN -- THIS IS WHERE ISSUES OF REGRET AND SOMETIMES FEELING LIKE A COMMODITY COME INTO THIS.

IT SHOULD BE MENTIONED THAT RIGHT NOW THE AVERAGE COMPENSATION FOR EGG DONATION IN THIS COUNTRY IS $7,000, AND IT VARIES BETWEEN ABOUT 5,000 TO 10,000, BUT THERE ARE, I'M SURE YOU'RE ALL AWARE, SOME QUITE EXTREME OFFERS FOR EGG DONATION.

ROBERTA NESS GAVE AN OVERVIEW OF CANCER

RISKS, AND SHE HAS PUBLISHED EXTENSIVELY ON THIS. AND MOST OF THE DATA ARE ON OVARIAN CANCER. IT'S IMPORTANT TO REALIZE AND RECOGNIZE THAT THE DATA ARE QUITE SOLID WITH REGARD TO INFERTILITY. HAVING INFERTILITY AS A WOMAN INCREASES THE RISK, HER RISK, OF OVARIAN CANCER. AND THE DATA ARE QUITE SOLID THAT THE OVULATION INDUCTION MEDICATIONS ARE NOT ASSOCIATED WITH AN INCREASED RISK OF OVARIAN CANCER.

THERE IS NO EVIDENCE THAT FERTILITY DRUGS INCREASE BREAST CANCER RISK. AND WITH REGARD TO UTERINE OR ENDOMETRIAL CANCER, THESE DATA ARE INCONCLUSIVE BECAUSE THE FOLLOW-UP IS ONLY AT THE TEN-YEAR POINT, AND SO THE JURY IS OUT AT THIS POINT. EFFECTS OVER TIME STILL NEED TO BE DETERMINED.

DR. PETERS: WOULD YOU ACCEPT A QUESTION IN THE MIDDLE HERE? ON THIS EVIDENCE IS IN WITH INFERTILITY INCREASES THE RISK OF OVARIAN CANCER, IS IT INFERTILITY PER SE, OR IS IT THE FACT THAT THE WOMAN ACTUALLY DOESN'T BEAR A CHILD DURING THIS PERIOD OF TIME? IN OTHER WORDS, IS IT INFERTILITY OR JUST THE LACK OF HAVING GOING THROUGH THE PROCESS OF A PREGNANCY?

DR. GUIDICE: THERE ARE SOME DATA FROM ALICE WHITTEMORE LOOKING AT DIFFERENT DIAGNOSES OF INFERTILITY, AND HER DATA DEMONSTRATE THAT EVER HAVING

BEEN PREGNANT, NOT NECESSARILY DELIVERING, BUT EVER HAVING BEEN PREGNANT IS PROTECTIVE AGAINST OVARIAN CANCER. SO HERE THE DATA, THERE'S A WHOLE RANGE OF EXPOSURES, IF YOU WILL, WOMEN WHO HAVE INFERTILITY AND NEVER BEEN PREGNANT, WOMEN WHO HAVE BEEN PREGNANT, BUT HAVE MISCARRIED, BUT HAVE NOT HAD CHILDREN. IT'S PRIMARILY THOSE TWO GROUPS.

DR. PETERS: THANKS.

DR. GUIDICE: WITH REGARD TO FUTURE FERTILITY, THERE'S NO CONVINCING EVIDENCE THAT ADHESIONS AND ANTI-OVARIAN ANTIBODIES ARE INCREASED WITH OVULATION INDUCTION. THERE'S SOME THEORETICAL BASIS FOR ESPECIALLY THE ANTI-OVARIAN ANTIBODIES BECAUSE IF YOU HAVE MANY POTENTIAL TARGETS AS THESE FOLLICLES ARE OPENING, THEY'RE NOT HUGE GAPING HOLES, BUT YOU COULD THEORETICALLY HAVE AN INCREASE IN ANTI-OVARIAN ANTIBODIES, AND THERE'S NO EVIDENCE OF THAT. THE EVIDENCE DOES ALSO NOT SUPPORT DEPLETION OF THE FOLLICLE POOL OR AN EARLY MENOPAUSE. SO THAT'S WHERE WHEN WE TALKED ABOUT HOW A GROUP OF FOLLICLES GETS GOING FOR A PARTICULAR CYCLE, WHAT THESE MEDICATIONS DO IS ESSENTIALLY PREVENT THE DYING OFF OF THE FOLLICLES THAT WOULD HAVE DIED OFF AS OPPOSED TO RECRUITING MORE AND MORE AND MORE. AND SO THERE IS NO EVIDENCE TO DATE THAT WOMEN WHO UNDERGO THESE

PROCEDURES HAVE AN EARLY MENOPAUSE. AND THE DATA ARE NOT COMPELLING REGARDING AN INCREASED RISK OF OVULATION INDUCTION AND EGG RETRIEVAL ON COMPROMISED FUTURE FERTILITY.

CHAIRMAN LO: LINDA, I'M SORRY. COULD I ASK AGAIN FOR CLARIFICATION? I KNOW YOU WERE VERY CAREFUL ABOUT THE WORDING HERE. SO NO CONVINCING EVIDENCE OF AN INCREASE IN ADHESIONS, THAT'S NOT THE SAME AS SAYING THERE'S EVIDENCE THAT THERE ARE NO ADHESIONS; IS THAT RIGHT? YOU'RE NOT SAYING THAT THERE'S EVIDENCE THAT IT DOESN'T HAPPEN. YOU'RE JUST SAYING THERE'S NO EVIDENCE THAT IT HAPPENS?

DR. GUIDICE: THERE IS NO EVIDENCE THAT IT HAPPENS.

CHAIRMAN LO: YOU HAVEN'T DISPROVED THAT IT CAN HAPPEN OR THAT THERE'S AN ASSOCIATION?

DR. GUIDICE: CORRECT. YES.

DR. TAYLOR: HAS THERE ACTUALLY BEEN A STUDY OF THIS? I'M NOT AWARE OF ANY SPECIFIC EVALUATION OF THAT.

DR. GUIDICE: NO.

DR. TAYLOR: I'VE SEEN SOME LOOKING AT SORT OF THE RECRUDESCENCE OR PROGRESSION OF ENDOMETRIOSIS FOLLOWING THE HORMONAL STIMULATION, BUT I DON'T THINK I'VE READ A STUDY THAT LOOKS AT ADHESION FORMATION

AFTER IVF AS OPPOSED TO BEFORE.

DR. GUIDICE: CORRECT. WHICH TIES INTO WHY THIS IS WORDED THE WAY IT IS.

HOW DO WE MINIMIZE RISKS? AND IF YOU HAVE A HANDOUT, THIS SLIDE IS IN THE HANDOUT. AND I WAS ASKED BY BOTH GEOFF AND BERNIE TO ADD SPECIFIC SLIDES ABOUT MINIMIZING THE MOST COMMON COMPLICATION, WHICH IS OHSS.

DR. LOMAX: I'M SORRY. TO MAKE ONE CLARIFICATION, WE WERE NOT ABLE TO UPDATE THE SLIDE DECK IN TIME. THESE SLIDES DID COME IN TOWARDS THE END. I APOLOGIZE. WE DON'T HAVE SLIDES AVAILABLE IN YOUR HANDOUT, BUT WE WILL MAKE THEM AVAILABLE. I THINK SOME OF THEM MAY BE MISSING, AND WE WILL UPDATE THOSE.

DR. GUIDICE: MINIMIZING RISK, IT'S VERY IMPORTANT FOR SUBJECT SELECTION AND TAKING A CAREFUL HISTORY. IDENTIFYING WHO IS AT RISK BY TRANSABDOMINAL OR TRANSVAGINAL ULTRASOUND TO LOOK AT HOW MANY FOLLICLES ARE THERE. IT'S CALLED THE ANTRAL FOLLICLE COUNT. USUALLY THOSE ARE THE FOLLICLES THAT DEVELOP. AND IF YOU SEE 50 FOLLICLES IN EACH OVARY, THAT'S NOT A GOOD CANDIDATE FOR OVULATION INDUCTION BECAUSE OF THE RISK OF OVARIAN HYPERSTIMULATION.

UTERINE FIBROIDS, OVARIAN ENDOMETRIOMAS ARE AT RISK FOR INCREASED INFECTION AND OTHER THINGS. EXCLUDING WOMEN WITH A HISTORY OF SEVERE ENDOMETRIOSIS.

THESE ARE SOME OF THE EXCLUSION CRITERIA THAT ARE APPLIED BY SOME OF THE LARGER EGG DONATION PROGRAMS, SUCH AS THE ONE AT CORNELL THAT DR. ROSENWAKS, WHO WAS ON THE COMMITTEE, SHARED WITH US.

THERE'S ALSO, AND I HAVE BROUGHT COPIES FOR ALL MEMBERS OF THE COMMITTEE, THE PRACTICE COMMITTEE REPORT ON OVARIAN HYPERSTIMULATION SYNDROME FROM THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE BECAUSE I THINK THIS WILL BE OF HELP TO YOU AS YOU DECIDE WHICH DIRECTION TO GO WITH REGARD TO RISKS OF OHSS.

SO MINIMIZING RISK FOR GENERALLY YOUNG WOMEN, SO EGG DONATION IS USUALLY DONE IN YOUNG WOMEN, USUALLY LESS THAN 30 YEARS OLD, AND THESE ARE THE WOMEN WHOSE OVARIES TEND TO HAVE MORE FOLLICLES THAN OLDER WOMEN. BUT EGG DONATION PROGRAMS EXCLUDE GENERALLY WOMEN WITH A HISTORY OF SEVERE ENDOMETRIOSIS, A HISTORY OF PELVIC INFLAMMATORY DISEASE, ABDOMINAL SURGERY WITH KNOWN PELVIC ADHESIONS, THROMBOPHILIAS OR ABNORMALITIES IN BLOOD COAGULATION AND BLEEDING, OVARIAN TUMORS, IRREGULAR MENSTRUAL BLEEDING BECAUSE IT'S UNCLEAR. A WOMAN COULD BE PREGNANT, SHE COULD HAVE A CANCER IN THE LINING OF THE UTERUS, A NUMBER OF THINGS COULD BE GOING ON. AND ALSO WOMEN WITH POLYCYSTIC OVARY SYNDROME. SO POLYCYSTIC OVARY SYNDROME IS A CLINICAL DISORDER WHERE WOMEN TEND TO OVULATE INFREQUENTLY. ABOUT HALF OF

WOMEN WHO HAVE THAT DISORDER ARE OVERWEIGHT. AND FOR THE MOST PART, THEY HAVE WHAT'S CALLED POLYCYSTIC-APPEARING OVARIES, SO THEY HAVE MORE OF THOSE LITTLE FOLLICLES IN THE OVARIES THAN WOMEN WHO DO NOT HAVE POLYCYSTIC OVARY SYNDROME.

THERE'S ALSO SOMETHING CALLED POLYCYSTIC-APPEARING OVARIES. I SHOULD MENTION WOMEN WITH THIS SYNDROME ALSO USUALLY HAVE ELEVATED LEVELS OF THE MALE HORMONE TESTOSTERONE AND FREQUENTLY HAVE INSULIN RESISTANCE, IF NOT FRANK DIABETES. THERE'S ALSO ANOTHER CONDITION CALLED POLYCYSTIC-APPEARING OVARIES WHERE THE OVARIES LOOK CHOCK FULL OF THESE LITTLE FOLLICLES, BUT THE WOMEN DO NOT HAVE THE HIGH TESTOSTERONE OR THE HIGH INSULIN OR TENDENCY TOWARDS DIABETES, AND THEY MAY OR MAY NOT BE OBESE, BUT IT STILL PUTS THEM INTO A HIGHER RISK CATEGORY BECAUSE THE FOLLICLES ARE SITTING READY TO TAKE OFF WHEN STIMULATED.

MINIMIZING RISK, DOUBLE CONTRACEPTION FOR OVUM DONORS. IF AN OVUM DONOR DONATES HER EGGS AND THERE MIGHT BE ONE OR TWO STILL HANGING AROUND THE PELVIS, IT'S POSSIBLE HER FALLOPIAN TUBES CAN PICK UP ONE OR TWO OF THEM; AND IF SHE HAS INTERCOURSE, SHE IS AT RISK FOR PREGNANCY, AND SO MOST PROGRAMS RECOMMEND DOUBLE CONTRACEPTION FOR THE OVUM DONOR AND ALSO FOR

HER PARTNER.

AND ALSO INCLUDING GENETIC AND SEXUALLY TRANSMITTED INFECTION SCREENING WITH STANDARD SCREENS. THESE ARE PRIMARILY FOR PURPOSES OF REPRODUCTION; BUT ALSO WITH REGARD TO INFECTION, ONE WOULD NOT WANT TO BE GOING THROUGH THE BACK OF THE VAGINA IF THERE WERE A RIP-ROARING INFECTION IN THE VAGINA THAT COULD PREDISPOSE TO EITHER INFECTION IN THE UPPER TRACK OR BLOOD INFECTION.

DR. ROWLEY: I WAS CURIOUS AS TO WHAT KIND OF GENETIC SCREENING WOULD DONE IN A STANDARD WAY.

DR. GUIDICE: WE TYPICALLY SCREEN FOR CYSTIC FIBROSIS, FOR MORE COMMON GENETIC DISORDERS, IF YOU WILL. AND THIS IS ALSO WHERE FAMILY HISTORY BECOMES VERY IMPORTANT IN SCREENING THE DONORS BECAUSE THAT WILL THEN DETERMINE ADDITIONAL GENETIC SCREENING.

SO SPECIFICALLY TO MINIMIZE OHSS, AND THESE ARE COMMENTS THAT HAVE COME DIRECTLY FROM THE REPORT THAT WERE DISCUSSED AT THE MEETING, ONE IS SUBJECT SELECTION AND CAREFUL HISTORY. ANOTHER IS, AGAIN, IDENTIFYING WHO IS AT RISK. TRANSVAGINAL ULTRASOUND TO ASSESS THE ANTRAL FOLLICLE COUNT. YOUNG, HEALTHY OVARIES TEND TO HAVE BETWEEN 10 AND 15 FOLLICLES PER OVARY. AND THE NUMBER OF EGGS RETRIEVED, SORT OF A RULE OF THUMB, IS ABOUT EQUAL TO THE ANTRAL FOLLICLE

COUNT PLUS OR MINUS TWO. EXCLUDING WOMEN WITH A HISTORY OF POLYCYSTIC OVARY SYNDROME OR POLYCYSTIC-APPEARING OVARIES AND NORMAL HORMONAL PARAMETERS. INDIVIDUALIZATION OF TREATMENT PROTOCOLS. AND THIS IS A VERY IMPORTANT ISSUE. ONE SIZE DOES NOT FIT ALL. WOMEN HAVE VERY DIFFERENT RESPONSES OF THEIR OVARIES TO THESE STIMULATORY MEDICATIONS. SOME WOMEN NEED VERY HIGH LEVELS IN ORDER TO GET TWO FOLLICLES TO DEVELOP, AND OTHERS NEED MAYBE ONE-FOURTH THAT PARTICULAR DOSE TO GET TEN FOLLICLES TO DEVELOP.

AND SO YOU REALLY NEED TO HAVE AN EXPERIENCED PHYSICIAN WHO IS CARING FOR THE PATIENT AND DOING THE STIMULATION WHO KNOWS AND UNDERSTANDS AND LOOKS AT THE ANTRAL FOLLICLE COUNT, TAKES INTO ACCOUNT THE AGE OF THE SUBJECT, AND CERTAINLY HER RISK AND ANY ASSOCIATED MEDICAL CONDITIONS. CAREFUL MONITORING IS IMPORTANT. AND SO THAT MEANS FREQUENT ULTRASOUNDS TO BE SURE THAT FOLLICLES ARE NOT JUST INCREASING IN NUMBERS, AND SOMETIMES ESTRADIOL LEVELS ARE ALSO DONE. SO PERIPHERAL CIRCULATING BLOOD LEVELS OF ESTROGEN, AND ESTROGEN IS MADE BY THE FOLLICLES AS THEY GROW. THE BIGGER THEY GET, THE MORE ESTROGEN. AND THERE ARE SOME DATA ON THE HIGHER -- QUITE A BIT OF DATA ON THE HIGHER THE ESTROGEN LEVEL, THE HIGHER THE RISK OF OHSS.

SO ONE POSSIBILITY, IF ONE REALLY WANTS TO GO

WITH A CYCLE, AND THERE REALLY ARE DIFFERENT MOTIVATIONS, AND WE DISCUSSED THIS IN TERMS OF EVEN THOUGH THERE MAY BE A RISK OF OHSS, IF A COUPLE WANTS TO GET PREGNANT AND THEY'VE INVESTED A LOT OF TIME AND ENERGY AND MONEY, THEY MAY BE WILLING TO TAKE A RISK OF A MILD FORM OR MODERATE. AND SO MOST TEAMS WOULD USE A LOWER DOSE OF HCG. HOWEVER, IF A WOMAN IS AT AN OBVIOUS HIGH RISK FOR OHSS, THE STANDARD OF CARE WOULD BE TO WITHHOLD HCG FOR EGG MATURATION.

THERE ARE JUST A COUPLE OF REPORTS OF USING LH AS THE TRIGGER, WHICH IS THE NATURAL THING IN THE BODY. IT HAS A VERY SHORT HALF-LIFE, ABOUT 20 MINUTES, AS OPPOSED TO HCG, WHICH IS SEVERAL HOURS. AND SO THIS IS ANOTHER POSSIBILITY TO TRIGGER EGG MATURATION AND HOPEFULLY TO MINIMIZE THE EFFECTS OF HCG ON OHSS.

IN ADDITION, IDENTIFYING AND EXCLUDING FROM PARTICIPATION AND STIMULATION WOMEN AT RISK. INDIVIDUALIZING THE STIMULATION PROTOCOL, SO THIS IS A SUMMARY, WITH IDEAL MINIMAL STIMULATION. AND THIS, OF COURSE, BRINGS UP ISSUES NOT ONLY FOR FERTILITY, BUT CERTAINLY FOR EGG DONATION, AS WE'LL GET INTO ON THE NEXT SLIDE, WITH REGARD TO WHAT ARE THE IDEAL TARGETS FOR NUMBERS OF EGGS IN A RESEARCH SETTING. A LOW THRESHOLD FOR CYCLE CANCELLATION BECAUSE THE PATIENT ALWAYS COMES FIRST. AND THERE ARE SOME DATA USING A

VASCULAR ENDOTHELIAL GROWTH FACTOR, ALSO KNOWN AS VPF OR VASCULAR PERMEABILITY FACTOR. THIS IS THE FACTOR THAT THE CELLS AROUND THE EGG MAKE IN RESPONSE TO HCG. AND SO WHEN HCG IS GIVEN, THERE'S A LOT OF THIS THAT'S MADE. AND THIS IS WHAT'S RESPONSIBLE FOR THE FLUID SHIFTS THAT OCCUR INTO THE ABDOMEN WHEN VERY HIGH LEVELS OF VEGF ARE AROUND. THAT'S EXPERIMENTAL.

WITH REGARD TO THE DATA FOR THESE OBSERVATIONS, IT'S VERY IMPORTANT TO NOTE, AND THIS WAS DISCUSSED EXTENSIVELY AT THE COMMITTEE, THAT THE STUDIES ARE LIMITED BY RELATIVELY SMALL NUMBERS OF SUBJECTS EXCEPT IN THE OVARIAN CANCER STUDIES. THE DATA THAT WE DO HAVE ARE ON PATIENTS, INFERTILITY PATIENTS, AND ARE NOT ON HEALTHY VOLUNTEERS FOR THE MOST PART, WHICH IS THE EGG DONOR POOL WHO MAY HAVE EITHER DECREASED OR INCREASED RISKS. ALSO, THE DATA ARE PRIMARILY ON CAUCASIAN WOMEN, MIDDLE TO UPPER SOCIOECONOMIC STATUS BECAUSE THESE ARE PRIMARILY THE WOMEN WHO CAN AFFORD TO HAVE IN VITRO FERTILIZATION FOR FERTILITY THERAPY.

AND INTERESTINGLY, DESPITE GREATER THAN 20 YEARS OF IVF, WE DO NOT HAVE A DATABASE ON HEALTH OUTCOMES OF WOMEN OR MEN UNDERGOING THESE PROCEDURES; AND, THUS, WE CANNOT DRAW INFORMATION ABOUT LONG-TERM RISKS FROM THE GREATER THAN ONE MILLION IVF CYCLES OVER

THE PAST 20 YEARS IN THE UNITED STATES AND CANADA. AND THAT IS FOR A VARIETY OF REASONS, PRIMARILY FINANCIAL. AND THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE, WHICH IS AN ORGANIZATION, THAT'S A PROFESSIONAL ORGANIZATION PRIMARILY FOR FERTILITY, BUT NOW ALSO FOR WOMEN'S HEALTH, IS VERY AWARE OF THIS. AND AT LEAST THEY'RE DISCUSSING IT. AND I SHOULD HAVE FULL DISCLOSURE THAT I AM ON THEIR BOARD OF DIRECTORS. I AM NOT ADVOCATING THEIR POLICY. I'M JUST REPORTING ON IT.

THE CHALLENGES FOR THE FUTURE ARE REALLY THE QUANTIFICATION OF RISK. YOU'VE SEEN THE WIDE VARIABILITY OF RISK FOR SEVERE OVARIAN HYPERSTIMULATION SYNDROME, FOR INSTANCE. THE INCLUSION AND EXCLUSION CRITERIA REALLY FORM A COMPLEX MATRIX, ESPECIALLY WHEN WE ARE LOOKING AT YOUNG EGG DONORS FOR RESEARCH. LONG-TERM OUTCOMES, HEALTH OUTCOMES OF FERTILITY, CANCER, PSYCHOLOGICAL ISSUES, DEMOGRAPHICS IN THE DONOR EGG POPULATION. SHOULD DONORS BE WOMEN WHO HAVE PREVIOUSLY HAD A CHILD OR NULLIPAROUS WOMEN SUITABLE TO DONATE FOR RESEARCH? SO WOMEN WHO HAVE NOT HAD A CHILD, WHAT IS THE OPTIMAL AGE FOR EGG DONATION FOR RESEARCH? IS IT REPRODUCTIVE AGE, 18 TO 45? IS IT REPRODUCTIVE DONOR AGE, WHICH IS CURRENTLY THE STANDARD, SOMEWHERE 21 AND 34, MORE COMMONLY 21 TO 30 YEARS OF AGE?

ANOTHER QUESTION THAT ARISES IS HOW MANY TIMES TO DONATE? THERE ARE YOUNG WOMEN WHO GO THROUGH SIX, SEVEN, EIGHT, NINE, TEN TIMES TO DONATE THEIR EGGS FOR MONEY AND FOR FERTILITY THERAPY. THE QUESTION, I THINK, CERTAINLY NEEDS CONSIDERATION FOR THE EGG DONOR POPULATION FOR RESEARCH.

HOW MUCH STIMULATION? HOW DO WE TAILOR THE PROTOCOLS? WHICH PROTOCOLS SHOULD WE USE? AND THERE ARE DIFFERENT PROTOCOLS. I DIDN'T GET INTO THEM. AND WE DISCUSSED THEM A LITTLE BIT AT THE MEETING, BUT THERE ARE WAYS TO MINIMIZE STIMULATION, BUT ALSO THERE ARE WAYS TO MAXIMIZE STIMULATION IN WOMEN WHO ARE POOR RESPONDERS.

WHAT'S THE TARGET NUMBER OF EGGS RETRIEVED? IN IVF CYCLES FOR FERTILITY, IT'S USUALLY SOMEWHERE BETWEEN 10 TO 12, MAYBE 15. IS THAT THE SAME NUMBER WE SHOULD BE THINKING ABOUT FOR EGG DONORS FOR RESEARCH? AND IS THERE A PEAK ESTRADIOL LEVEL THAT SHOULD BE TARGETED? ANOTHER QUESTION THAT WAS ENTERTAINED AT THE COMMITTEE WAS ARE DONORS WITH A CHRONIC DISEASE A GOOD RESOURCE FOR OOCYTES FOR RESEARCH?

SO ONE WAY TO ADDRESS THE ISSUE OF RISK AND TO MINIMIZE RISK IS TO GET AN ALTERNATIVE SOURCE OF EGGS, AND WE DISCUSSED THIS AS WELL. WE TALKED ABOUT IMMATURE EGGS FROM IVF CYCLES. ABOUT 20 PERCENT OF THE

EGGS THAT ARE OBTAINED ARE USUALLY NOT MATURE ENOUGH, AND THESE ARE USUALLY NOT USED OR THEY DON'T FERTILIZE. AND THESE, HOWEVER, LIKELY WOULD NEED TO BE MATURED IN VITRO. AND I SAY LIKELY BECAUSE IT'S REALLY NOT CLEAR AT WHAT STAGE OF OOCYTE DEVELOPMENT SOMATIC CELL NUCLEAR TRANSFER, FOR INSTANCE, CAN BE INITIATED USING A HUMAN EGG, ALTHOUGH FOR FERTILIZATION AND GENERATION OF AN EMBRYO AND, THEREFORE, AN INNER CELL MASS AND, THEREFORE, HUMAN EMBRYONIC STEM CELL LINES, THERE WOULD NEED TO BE IN VITRO MATURATION.

THERE ARE ALSO FAILED-TO-FERTILIZE OOCYTES FROM IVF PROCEDURES, SO THESE ARE MATURE EGGS WHERE THERE'S EITHER AN ISSUE WITH THE EGG ITSELF OR MORE COMMONLY WITH THE SPERM. AND THESE CYCLES USUALLY RESULT IN NO EMBRYOS, AND SO THOSE EGGS ARE AVAILABLE OR COULD BE AVAILABLE FOR RESEARCH. AND SO THESE ARE ALL IN WOMEN UNDERGOING THERAPIES FOR FERTILITY, THE FIRST TWO BULLETS. THE THIRD IS WHEN A WOMAN UNDERGOES PELVIC SURGERY, IF SHE WOULD CONSENT TO SOME OF THE OUTER PORTION OF HER OVARY, A SMALL PORTION OF IT, TAKEN OUT OR TO HAVE SOME OF HER FOLLICLES THAT ARE IN THE OVARY PUNCTURED AT THAT TIME AND EGGS RETRIEVED. THESE EGGS ALSO WOULD LIKELY NEED TO BE MATURED IN VITRO. AND THE WHOLE ISSUE OF IN VITRO MATURATION WAS DISCUSSED BY CATHERINE RACOWSKY, THE EMBRYOLOGIST FROM

HARVARD, WHO WAS ON THE COMMITTEE AND AT THE WORKSHOP, AND IT'S NOT A TRIVIAL PROCESS AND IS ACTUALLY NOT VERY WELL WORKED OUT. SO WHILE THESE ARE INTERESTING ALTERNATIVE SOURCES, THESE ARE NOT SURE DEALS.

WE ALSO DISCUSSED CADAVERIC SOURCES AND ISSUE OF CONSENT FROM FAMILIES, NEXT OF KIN AT THE TIME OF DURESS, ASKING NEXT OF KIN FOR GAMETES. AN ADVANCED DIRECTIVE. I'M NOT SURE THAT THERE ARE MANY PEOPLE WHO USE AN ADVANCE DIRECTIVE WITH REGARD TO THE DISPOSITION OF THEIR EGGS IN THE EVENT OF A DEMISE. AND, OF COURSE, HOW VIABLE WOULD THE OOCYTES BE AFTER OTHER ORGANS ARE HARVESTED? USUALLY THE MAJOR ORGANS, LIKE THE LIVER AND THE KIDNEY FOR TRANSPLANTATION WHERE THEY ARE SAVING LIVES, ARE THE ONES THAT ARE HARVESTED FIRST. AND SO IT'S UNCLEAR, IN FACT IT'S UNTESTED, THE VIABILITY OF EGGS AFTER PERHAPS SEVERAL HOURS FOR USE IN RESEARCH.

WE ALSO DISCUSSED OOCYTES FROM FETAL OVARIES, AND THESE ARE VERY HARD TO FIND. COMMONLY THEY WOULD COME FROM ABORTED SPECIMENS. AND, AGAIN, THESE ARE VERY, VERY RARE. AND THEN PERHAPS ONE OF THE BRIGHTEST PARTS ON THE HORIZON IS OOCYTE GENERATION FROM GERM CELLS DERIVED FROM HUMAN EMBRYONIC STEM CELLS. AND SO IT'S SOMEWHAT OF A VICIOUS CYCLE IN THAT ONE WOULD NEED THE HUMAN EMBRYONIC STEM CELL TO GENERATE A GERM CELL

AND THEN DIFFERENTIATE THAT GERM CELL TO BECOME A GAMETE SUCH AS AN EGG.

SO I WILL STOP THERE. THAT'S A SUMMARY OF EVERYTHING WE TALKED ABOUT. THE REPORT IS SHOWN HERE. YOU CAN LOOK AT IT ON THE WEBSITE. AND I DID WANT TO THANK THE COMMITTEE MEMBERS SHOWN HERE AND ALSO THE MEMBERS OF THE NAS STAFF WHO WERE EXTREMELY HELPFUL IN MOVING THIS PROCESS ALONG IN A VERY SHORT TIMELINE AND GETTING THE REPORT OUT TO THE CIRM IN A VERY TIMELY FASHION. THANK YOU.

CHAIRMAN LO: LINDA, THANK YOU SO MUCH BOTH FOR CHAIRING THE COMMITTEE AND MAKING SUCH A WONDERFUL PRESENTATION. ARE THERE QUESTIONS FOR DR. GUIDICE?

DR. OLDEN: IT SEEMS TO ME THAT A NUMBER OF ONE TO TWO PER THOUSAND, I BELIEVE THAT'S THE RISK FOR OHSS. THAT SEEMS TO BE HIGH TO ME. THAT NUMBER ISN'T DISTURBING TO YOU OR THE COMMITTEE?

DR. GUIDICE: IT DEPENDS. I'LL HAVE THE COMMITTEE MEMBERS CERTAINLY RESPOND, BUT IT'S GOING TO DEPEND ON THE STAGE OF THE OHSS.

DR. OLDEN: I'M SORRY. I DON'T UNDERSTAND THAT.

DR. GUIDICE: THE SEVERE. I CAN PULL THE SLIDE BACK UP.

DR. OLDEN: I GUESS WHAT I'D LIKE TO SEE IS

TO KNOW WHAT IS THE RISK FOR THE MODERATES BECAUSE THOSE ARE THE ONES THAT -- IF YOU BREAK THEM DOWN, IF YOU LUMP THEM ALTOGETHER, WHAT WOULD YOU SAY THE RISK IS? LET ME SAY FOR CANCER RISK, EPA STANDARDS IS ONE IN A MILLION. AND ONE OR TWO IN A THOUSAND IS A HUGE RISK FROM MY PERSPECTIVE.

DR. GUIDICE: WELL, LET'S GO TO THE MINIMUM FIRST. AND THE RISK OF THAT IS CLOSE TO 80 TO 90 PERCENT OF WOMEN, THE MINIMAL DISEASE, THE FIRST BULLET. THE MODERATE, I GUESS I WOULD GUESS AT THIS POINT THAT IT'S PROBABLY ABOUT, AND, ROB, HELP ME HERE IF YOU WOULD, I WOULD SAY MAYBE 15, 20 PERCENT.

DR. TAYLOR: I WAS THINKING 10 TO 20, SOMETHING LIKE THAT.

CHAIRMAN LO: DOES THAT NUMBER INCLUDE WOMEN WHO GO ON TO BECOME PREGNANT?

DR. GUIDICE: YEAH.

DR. TAYLOR: ABSOLUTELY.

CHAIRMAN LO: SO IF YOU WERE TO TRY AND QUANTIFY THE RISK IN WOMEN WHO HAVE OOCYTE RETRIEVAL, BUT THEN DO NOT GET PREGNANT, DO NOT HAVE THE INCREASE IN ESTRADIOL AND PROGESTERONE, CAN YOU TRY AND PUT A QUANTIFICATION ON THAT RISK?

DR. TAYLOR: I'VE NOT SEEN REPORTED DATA, AND I HAVEN'T BEEN IN PROGRAMS WHERE THERE'S BEEN A HUGE

DONOR POPULATION. SOMEONE LIKE ZEV ROSENWAKS OR THE GROUP AT COLUMBIA WHERE THEY HAVE A LOT OF DONORS WOULD PROBABLY BE BEST. I WOULD THINK THAT THE RISK IS AT LEAST FIVEFOLD LOWER IN PATIENTS WHO AREN'T SUBJECTED TO THE SUPERSEDING EFFECTS OF A PREGNANCY. SO THAT WOULD JUST BE KIND OF A GUESSTIMATE, BUT IT'S FAIRLY UNUSUAL, I THINK, IN THAT POPULATION.

DR. OLDEN: THE OTHER QUESTION I HAVE IS THAT FROM THE POINT OF VIEW OF THIS INITIATIVE HERE IN CALIFORNIA, SHOULDN'T WE SET THE RISK, THE ACCEPTABLE RISK, FOR AN EGG DONOR TO BE MUCH -- TO MAKE SURE IT'S MUCH LESS THAN THAT FOR SOMEBODY WHO'S UNDERGOING THE PROCEDURES FOR IN VITRO FERTILIZATION PURPOSES AND REPRODUCTION? I MEAN A YOUNG WOMAN WHO'S JUST GOING IN TO DONATE EGGS FOR RESEARCH OR FOR SOMEONE ELSE, SHOULDN'T THAT RISK BE -- SHOULDN'T WE REQUIRE THAT THE RISK FOR THAT INDIVIDUAL BE MUCH LOWER THAN FOR SOMEBODY WHO, FOR THEIR OWN BENEFIT, IS HAVING THIS PROCEDURE DONE FOR REPRODUCTIVE PURPOSES? THE RISK SHOULDN'T BE THE SAME FOR THOSE TWO PEOPLE BECAUSE THE BENEFIT TO THE DONOR WHO'S JUST DONATING EGGS FOR PAY OR FOR WHATEVER OTHER PURPOSES, WE SHOULD BE VERY CAREFUL TO PROTECT THE HEALTH OF THAT INDIVIDUAL, MAKE SURE THAT THE RISKS ARE MINIMAL IN THIS CASE.

DR. GUIDICE: I GUESS THAT'S A COMMITTEE

DISCUSSION. I AGREE WITH YOU, AND THAT IS ONE OF THE REASONS THAT ON THE SLIDES ABOUT MINIMIZING THE RISK THERE WAS ALSO -- I'LL JUST GET TO THOSE -- BUT THERE WAS, AGAIN, A COMMENT ABOUT A LOW THRESHOLD FOR CANCELLATION. AND THERE'S A DIFFERENCE BETWEEN A COUPLE WANTING TO GET PREGNANT, AGAIN NOT AT MAJOR RISK FOR HEALTH, BUT THAT CERTAINLY IS SOMETHING THAT DESERVES CONSIDERATION.

DR. OLDEN: AND THE OTHER ISSUE THAT I HAVE IS ABOUT THIS RELATIONSHIP BETWEEN INFERTILITY OVULATION AND OVARIAN CANCER RISK. IN THE CASE OF INFERTILITY AND OVULATION, THE OVARIES HYPERTROPHY. THERE'S NO EVIDENCE THAT THE OVARIES GROW, ENLARGE. IN THE CASE OF THIS PROCEDURE, THEY DO. SO IS COMPARING WHAT HAPPENS IN A CASE OF INFERTILITY AND OVULATION WITH OVARIAN CANCER RISK VERSUS WHEN YOU ADMINISTER ALL THESE HORMONES TO INDUCE EGG MATURATION AND DEVELOPMENT, THE OVARIES ACTUALLY GROW TO BE MUCH LARGER. AND PRESUMABLY THE OVARIES WOULD PRODUCE MUCH MORE ESTROGEN, RIGHT?

DR. GUIDICE: YES.

DR. OLDEN: SO THE HORMONE LEVELS WOULD BE VERY DIFFERENT IN THIS CASE THAN IN A WOMAN WHO DIDN'T OVULATE, MY GUESS, BUT YOU MONITOR THAT. IS THAT THE CASE? AND THAT IS THE CASE, I THINK. YOU DID MONITOR

HORMONE LEVEL.

DR. GUIDICE: THE ESTROGEN LEVELS DO GO UP, AND THEY ARE -- AGAIN, IT'S TEMPORALLY RESTRICTED TO A COUPLE WEEKS. SO THE THEORETICAL CONSIDERATION FOR AN INCREASED RISK OF OVARIAN CANCER HAD TO DO WITH THE NUMBERS OF OVULATIONS AND SUBSEQUENT REPAIR OF THE SMALL AREA THAT THE EGG CAME OUT OF. AND THAT IF YOU HAD MANY OVULATIONS, YOU MAY HAVE A COUPLE OF THE REPAIR PROCESSES BECAUSE THERE ARE SO MANY THERE GOING ON AT THE SAME TIME THAT MIGHT GO AWRY. AND, THEREFORE, THE OUTSIDE OF THE OVARY, THE EPITHELIUM, MAY THEN RESULT IN CANCER. THAT DOESN'T SEEM TO BE -- FROM ALL THE DATA THAT HAVE BEEN REVIEWED, THE RISK OF OVARIAN CANCER DOESN'T SEEM TO BE RELATED TO UNDERGOING OVULATION INDUCTION BECAUSE IF YOU TAKE A POPULATION OF WOMEN WHO HAVE UNDERGONE OVULATION INDUCTION AND ARE INFERTILE AND YOU TAKE A POPULATION OF WOMEN WHO HAVE UNDERGONE OVULATION INDUCTION AND WHO ARE FERTILE, FOR INSTANCE WITH MALE FACTOR, THEN THE RISK OF OVARIAN CANCER IS IN THE INFERTILE POPULATION, NOT IN THE OTHER. SO THAT'S THE CONCLUSION. THAT'S ONE OF THE PIECES OF EVIDENCE.

DR. TAYLOR: I THINK THERE ARE A COUPLE OF COMMENTS. SO ONE IS WE'RE NOT REALLY CERTAIN, IT'S STILL KIND OF UNCLEAR WHAT THE SOURCE OF THE COMMON

OVARIAN CANCERS -- WHAT OVARIAN CELL IS ACTUALLY THE SOURCE. IN FACT, THERE'S SOME PEOPLE WHO THINK IT MIGHT NOT EVEN BE OVARIAN, BUT THAT'S GETTING A LITTLE BIT STRANGE. THE HORMONES THAT WE USE FOR OVULATION INDUCTION ARE, IN FACT, MITOGENS FOR THE GRANULOSIS CELLS, BUT GRANULOSIS CELL TUMORS ARE EXTREMELY RARE, AND THAT'S NOT ACTUALLY BEEN ASSOCIATED.

SO AS LINDA SUGGESTED, IT SEEMS LIKE IT'S THE SURFACE EPITHELIAL CELLS WHICH AREN'T ACTUALLY STIMULATED. THEY'RE NOT REALLY HORMONALLY RESPONSIVE. SO THOSE SEEM TO BE WHERE THE OVARIAN CANCERS ARISE FROM, AND THERE HASN'T BEEN A GOOD CORRELATION. SO LINDA SUGGESTED THAT YOU'VE GOT SORT OF FERTILE AND INFERTILE COUPLES, BUT THERE ARE ALSO WOMEN WITH LONG-TERM INFERTILITY WHO DIDN'T UNDERGO OVULATION INDUCTION WHO ARE AT INCREASED RISK OF OVARIAN CANCER. SO THE ORIGINAL HYPOTHESIS, I THINK, WAS THAT THIS IS ASSOCIATED WITH INFERTILITY AND, THEREFORE, IT'S PROBABLY ASSOCIATED WITH THE MITOGENIC ACTIVITIES OF THE HORMONAL MEDICATIONS THAT WE USE; BUT WHEN THEY'VE KIND OF GONE THROUGH THESE LARGE EPIDEMIOLOGIC STUDIES, AND THE GROUP AT STANFORD HAS BEEN REALLY QUITE INVOLVED IN SOME OF THOSE, IT REALLY SEEMS TO BE MORE ASSOCIATED WITH INFERTILITY THAN IT DOES WITH THE OVULATION INDUCING AGENTS.

I AGREE THAT IT SORT OF TELIOLOGICALLY WOULD MAKE SENSE THAT IT WOULD BE A HORMONE DRIVEN THING, BUT THAT DOESN'T SEEM TO BE THE CASE.

CHAIRMAN LO: IF I COULD, COULD I FOLLOW UP ON A QUESTION THAT DR. OLDEN RAISED BECAUSE HIS MIND THINKS MUCH FASTER THAN MINE DOES. IF YOU GO BACK TO THE OHSS SLIDE AND THE INCIDENCE OF IT, COULD I ASK THE QUESTION ON THE SEVERE OHSS, THE ONE IN A THOUSAND OR TWO IN A THOUSAND, AGAIN, MY UNDERSTANDING IS THAT FIGURE INCLUDES WOMEN WHO HAVE HORMONAL STIMULATION WITH HCG, BUT INCLUDES THOSE WHO GO ON TO BECOME PREGNANT. IF YOU JUST LOOK AT THE WOMEN WHO GET HCG OR RECOMBINANT LH, BUT DON'T GET PREGNANT, SO THIS WOULD BE THE DONOR POOL RATHER THAN A WOMAN TRYING TO GET PREGNANT HERSELF, DO WE KNOW WHAT THE INSTANCE OF SEVERE OHSS IS IN THAT POPULATION? PRESUMABLY IT'S LOWER THAN THE .1 TO .2. DO WE HAVE A SENSE OF HOW MUCH LOWER?

DR. GUIDICE: NO. THE DATA ARE REPORTED -- I WAS THINKING OF THE SART DATA. I DON'T THINK OHSS IS REPORTED AS PART OF A DATASET. AND SO ONE IS THEN LEFT WITH, AS LISTED, IN TERMS OF STUDY LIMITATIONS, WITH SMALL STUDIES, RETROSPECTIVE REVIEWS. AND SO IT WOULD HAVE BEEN MUCH BETTER HAD WE IN THESE ONE MILLION CYCLES AND OF THE 14,000 EGG DONOR CYCLES PER YEAR,

WITH THE FIRST ONE STARTING IN 1994, SO 13 YEARS NOW OF EGG DONOR CYCLES, SO IF WE DO THE MATH, IT'S A LOT OF CYCLES, IT WOULD HAVE BEEN GOOD TO HAVE HAD SOME ASSESSMENT OF EXACTLY THAT QUESTION AND BROKEN DOWN BY MINIMAL OR MODERATE AND SEVERE.

CHAIRMAN LO: DO WE EVEN KNOW THAT FROM SINGLE CENTER CASE SERIES, SAY AT THE CORNELL GROUP, HAVE THEY LOOKED AT THE INCIDENCE OF SEVERE OHSS IN DONORS WHO DON'T BECOME PREGNANT? THERE WOULD BE A BIG CONFIDENCE INTERVAL, BUT DO WE KNOW WHAT THE POINT ESTIMATE IS?

DR. GUIDICE: YES. ZEV ROSENWAKS, AND IT'S ACTUALLY IN THE REPORT AS WELL, COMMENTED THAT OF THE, I THINK IT WAS, 2,000 EGG DONORS THAT THEY HAVE DONE, I BELIEVE THAT'S THE NUMBER, THEY HAVE HAD ZERO SEVERE OHSS. AND PART OF THAT IS PATIENT SELECTION, LOW THRESHOLD FOR NOT GIVING HCG BECAUSE, AGAIN, YOU DON'T GET OHSS IF YOU DON'T GIVE HCG.

DR. TAYLOR: JUST A COMMENT ABOUT THE RECOMBINANT LH, WHICH IS REALLY A GREAT IDEA BECAUSE ALL IT TAKES IS REALLY A BRIEF STIMULATION OF THE LH RECEPTORS TO GET OVULATION TO OCCUR TO INDUCE THAT FINAL MATURATION THAT'S RESPONSIBLE, SO USING HCG WHICH HAS A HALF-LIFE OF ABOUT 24 HOURS RATHER THAN RECOMBINANT LH, WHICH HAS A HALF-LIFE OF AROUND 20

MINUTES, MAKES A LOT MORE SENSE, BUT IT'S NOT APPROVED IN THE U.S. THROUGH THE FDA. BUT I BELIEVE THAT THE EU FDA EQUIVALENT HAS ACTUALLY APPROVED IT IN EUROPE, SO THERE'S PROBABLY GOING TO BE SOME MORE EXPERIENCE WITH THAT, BUT UNFORTUNATELY THAT'S KIND OF AN EXPERIMENTAL SOLUTION FOR A DONOR POPULATION. I'M NOT SURE THAT WOULD BE A WISE RECOMMENDATION MAYBE TO MAKE AT THIS POINT.

DR. GUIDICE: LUVARIS, WHICH IS RECOMBINANT LH, WAS APPROVED BY THE COMMITTEE THAT I CHAIRED AT THE FDA ON REPRODUCTIVE HEALTH DRUGS. AND THE INDICATION FOR APPROVAL WAS FOR HYPOGONADOTROPHIC HYPOGONADISM, BUT IT CAN ALWAYS BE USED OFF LABEL. THERE ARE OTHER WAYS OF USING IT, BUT I HAVE NOT SEEN ANY -- THERE ARE NO LARGE RANDOMIZED CONTROL TRIALS OF USE OF THAT FOR THIS TYPE OF -- FOR FERTILITY THERAPY.

DR. ROWLEY: I JUST WANTED TO FOLLOW UP ON THIS QUESTION OF DATA BECAUSE IT'S UNDERSTANDABLE WHY THERE ARE NO DATA FROM THE UNITED STATES GIVEN OUR POOR HEALTHCARE SYSTEM. BUT I WOULD HAVE THOUGHT IN EUROPE, SCANDINAVIA, FOR EXAMPLE, BUT OTHER EUROPEAN COUNTRIES WHERE THERE ARE BETTER DATA, WHY AREN'T THERE ANY AVAILABLE FROM EUROPE ON THIS ISSUE OF WHAT'S THE FREQUENCY OF OHSS AND THE VARIOUS GRADES?

DR. GUIDICE: IT'S A GOOD QUESTION. I'M

TRYING TO THINK, AGAIN, I DON'T BELIEVE THAT, FOR INSTANCE, IN THE UK WHERE THE ENTIRE SYSTEM FOR THE INFRASTRUCTURE IS SUCH THAT THERE'S A LARGE AMOUNT OF DATA COLLECTION. I'M NOT AWARE AND I DON'T THINK ANYBODY IN THE COMMITTEE WAS AWARE OR THE PARTICIPANTS THAT THAT'S PART OF THE DATA ACQUISITION AND THE DATABASE.

ALSO, IT'S NOT CLEAR THAT -- WELL, I JUST DON'T KNOW WHETHER SOME PROGRAMS WOULD WANT TO REPORT SOME OF THEIR SEVERE. IF YOU PUT OUT A REPORT THAT IN OUR CASE SERIES, WE HAVE 8 PERCENT SEVERE OVARIAN HYPERSTIMULATION SYNDROME, I SERIOUSLY DOUBT THAT YOU'D HAVE VERY MANY PATIENTS GOING TO YOU. SO THAT MAY BE PART OF THE ISSUE. I DON'T KNOW.

DR. OLDEN: BUT FOLLOWING UP ON THAT COMMENT, I HAD THE SAME ISSUE BECAUSE I WOULD THINK THE SCANDINAVIAN COUNTRIES IN PARTICULAR, I'M NOT SURE THE UK, BUT THE SCANDINAVIANS, I BET YOU, HAVE THAT DATA. AND SO THEY MAYBE JUST HAVEN'T ANALYZED IT BECAUSE OBVIOUSLY THAT TAKES A LOT OF RESOURCES. BUT MAYBE THIS INITIATIVE SHOULD THINK ABOUT FUNDING A STUDY TO GET THAT DATA BECAUSE I CAN'T IMAGINE NORWAY DOESN'T HAVE IT. THEY HAVE A LOT OF WORK IN THIS AREA.

DR. TAYLOR: I'M CURIOUS, LINDA. DO YOU HAVE ANY IDEA ABOUT HOW WELL DEVELOPED THE EGG DONOR

BUSINESS IS OUTSIDE OF THE U.S.? I THINK MOST OF THE STUDIES THAT I'VE READ HAVE COME FROM U.S. CENTERS. I'M JUST SORT OF WONDERING WHETHER -- I MEAN A LOT OF SORT OF THE SCANDINAVIAN COUNTRIES, A LOT OF THE EUROPEAN COUNTRIES HAVE IVF AS A COVERED SERVICE IN THEIR HEALTHCARE SYSTEM. I DON'T KNOW ABOUT EGG DONATION. AND I'M JUST KIND OF CURIOUS. IT MIGHT BE THAT THERE ARE NOT AS MANY DATA AS WE'D LIKE ELSEWHERE IN THE WORLD EITHER.

DR. GUIDICE: COUNTRIES LIKE ITALY, FOR INSTANCE, WHERE ASSISTED REPRODUCTION WENT THROUGH A HEYDAY AND THEN ALMOST GROUND TO A HALT, EGG DONATION IS JUST NOT PART OF THE SERVICES RENDERED. I DON'T KNOW ABOUT -- IT CERTAINLY IS PART OF THE SERVICES RENDERED IN THE UK AND BELGIUM, WHICH HAS ONE OF THE MOST ADVANCED ART SYSTEMS. I DON'T KNOW ABOUT THE OTHER COUNTRIES. MY SENSE IS THAT IT'S NOT ALL THAT WELL DEVELOPED.

CHAIRMAN LO: ONE THING IS THAT MANY OF THE EU COUNTRIES DO NOT ALLOW PAYMENT BEYOND REIMBURSEMENT OF EXPENSES TO OOCYTE DONORS, SO THERE ARE VERY FEW WOMEN COMING FORWARD TO DONATE THEIR OOCYTES FOR CLINICAL IVF UNLIKE HERE.

DR. OLDEN: I HAVE ANOTHER CONCERN, IF YOU DON'T MIND. THAT WAS A GOOD REPORT, SO I'M NOT -- I

ENJOYED IT AND APPRECIATED IT. WHAT ARE WE DOING TO ENCOURAGE WOMEN FROM SOCIOECONOMIC DISADVANTAGED BACKGROUNDS, AND I'M THINKING HERE OF, I GUESS, THE WOMEN WHO WERE IN THE STUDY WERE MOSTLY UPPER INCOME, UPPER MIDDLE CLASS OR HIGHER. BUT BECAUSE I'M THINKING ABOUT NOT SO MUCH CO-MORBIDITIES BUT -- WELL, MAYBE CO-MORBIDITIES, BUT DIET, FOR EXAMPLE, MAY BE A VERY IMPORTANT FACTOR. THE IMMUNE SYSTEM, WHETHER ONE IS IMMUNE SUPPRESSED, MAY ALSO BE AN ISSUE. AND I ASSUME THESE WERE MAINLY CAUCASIAN WOMEN. WAS THAT THE CASE? WELL, AT LEAST THE LOW-INCOME CAUCASIAN WOMEN SHOULD ALSO BE LOOKED AT, AND WE SHOULD DO SOMETHING BECAUSE I REMEMBER WE SPENT A FAIR AMOUNT OF TIME DISCUSSING THAT ISSUE TO MAKE SURE THAT THE FULL SPECTRUM OF SOCIOECONOMIC CLASS AS WELL AS RACE BE INCLUDED.

NOW, GRANT YOU, SO WE HAVE TO DEVELOP SOME INITIATIVES TO ENCOURAGE THESE POPULATIONS TO DONATE EGGS, FOR EXAMPLE. SO I THINK THAT THE FACT THAT WE DON'T HAVE DATA ON CERTAINLY LOW-INCOME CAUCASIANS IS A WEAKNESS, AND WE SHOULD DO SOMETHING TO ENCOURAGE THAT, IT SEEMS, BECAUSE THESE PEOPLE ARE LIKELY TO BE MALNOURISHED, AND CERTAINLY THAT MAY HAVE SOME EFFECT ON THEIR RISK.

DR. GUIDICE: AND THE COMMITTEE DISCUSSED THE HEALTH DISPARITY IN TERMS OF DATA DISPARITY. AND

BECAUSE OUR CHARGE WAS NOT TO MAKE RECOMMENDATIONS, WE DID NOT MAKE RECOMMENDATIONS, BUT YOUR POINT IS EXTREMELY WELL TAKEN.

CHAIRMAN LO: ANY OTHER QUESTIONS FROM COMMITTEE MEMBERS? ANY QUESTIONS FROM ANYONE IN THE AUDIENCE?

DR. OLDEN: I HAVE ANOTHER ISSUE, BUT IT'S NOT FOR THE PRESENTER. IT'S FOR THE COMMITTEE TO DISCUSS, AND I WONDER WILL THERE BE OPPORTUNITY LATER ON TODAY OR TOMORROW TO DISCUSS THAT?

CHAIRMAN LO: ABSOLUTELY. IN FACT, WE'RE GOING TO SEGUE INTO THE DISCUSSION TO FOLLOW UP. DR. GUIDICE IS ACTUALLY ON HER WAY TO THE AIRPORT.

DR. OLDEN: IT WAS A GOOD PRESENTATION.

MR. REYNOLDS: WELL, IT'S NOT SO MUCH A QUESTION AS MUCH AS IT'S COMMENT ON A, I THINK, A CRITICAL PASSAGE HERE IN THE REPORT.

CHAIRMAN LO: JUST FOR THE RECORD, COULD WE --

MR. REYNOLDS: I JUST HOPE THIS IS THE APPROPRIATE TIME FOR SUCH A COMMENT. SO I'M JESSE REYNOLDS FROM THE CENTER FOR GENETICS AND SOCIETY. AND I JUST THINK IT'S IMPORTANT TO STEP BACK FROM THE REPORT AND LOOK AT -- ASK AND REFLECT ON WHY WE'RE LOOKING AT EGG DONATION FOR STEM CELL RESEARCH IN THE

FIRST PLACE. WHAT IS THE RELATIONSHIP BETWEEN EGG DONATION AND STEM CELL RESEARCH?

AND THE PASSAGE THAT'S USED ABOUT THREE TIMES IN THE REPORT SAYS -- THIS IS JUST FROM PAGE 7. IT'S IN A NUMBER OF DIFFERENT PLACES -- THE REQUIRED SUPPLY OF STEM CELLS ARE COLLECTED FROM DEVELOPING HUMAN EMBRYOS CREATED FROM EGGS OR OOCYTES HARVESTED FROM THE OVARIES OF FEMALE DONORS. THUS, MUCH OF THE PROMISE OF STEM CELLS DEPENDS ON WOMEN CHOOSING TO DONATE OOCYTES TO THE RESEARCH EFFORT.

AND GIVEN THAT, AS FAR AS I KNOW, ALL STEM CELL -- ALL EMBRYONIC STEM CELL LINES TO DATE WERE DERIVED FROM EMBRYOS LEFT OVER FROM IVF PROCEDURES. I DON'T KNOW OF ANY STEM CELL RESEARCH BEING CONDUCTED USING EMBRYOS CREATED THROUGH FERTILIZATION SPECIFICALLY FOR EMBRYONIC STEM CELL RESEARCH. THIS LIMITS THE USE OF EGGS DERIVED SPECIFICALLY FOR RESEARCH SOLELY TO SCNT, WHICH AT THIS POINT IN TIME HAS NOT DERIVED -- HAS NOT SUCCESSFULLY LED TO THE DERIVATION OF ANY STEM CELL LINES AND IS BEING CONDUCTED AT AN EXPERIMENTAL LEVEL IN ABOUT FIVE RESEARCH CENTERS IN THE U.S., AROUND THAT NUMBER, A HANDFUL. AND I JUST FEEL THAT THE WAY THAT THIS PASSAGE IS WORDED INDICATES THAT, AS IT CURRENTLY STANDS, THE DONATION OF EGGS SPECIFICALLY FOR RESEARCH

IS A CRITICAL PART OF MUCH OF THE PROMISE OF STEM CELLS, AS THIS SAYS, I THINK IS INACCURATE. I JUST WANT TO GET THAT ON THE RECORD. THANK YOU.

CHAIRMAN LO: THANK YOU. IF THERE ARE NO OTHER QUESTIONS, I'D LIKE TO THANK DR. GUIDICE AGAIN FOR THE REPORT AND ALSO FOR COMING AND PRESENTING THINGS SO CLEARLY AND ANSWERING OUR QUESTIONS. THANKS.

HOW DO YOU GUYS FEEL ABOUT TAKING A BREAK AND STRETCHING A BIT BECAUSE WE WANT TO TAKE WHAT THIS REPORT IS, AND THEN WE HAVE SOME SUGGESTIONS ON NEXT STEPS BUILDING OFF THIS REPORT. LET'S TAKE A TEN-MINUTE BREAK AND STRETCH OURSELVES.

(A RECESS WAS TAKEN.)

CHAIRMAN LO: OKAY. SO ON YOUR DESK IS A REPRINT OF THE ASRM GOOD PRACTICE GUIDELINES FOR PREVENTING OHSS, WHICH WAS IN *FERTILITY AND STERILITY* LAST NOVEMBER. OKAY. SO WHAT I WANT TO DO IS SORT OF BUILD UPON THIS PRESENTATION BY DR. GUIDICE AND THE IOM REPORT, AND TO SAY THAT OBVIOUSLY THERE IS A LOT OF INTEREST IN TRYING TO DERIVE SCNT-RELATED LINES. THAT WAS PART OF THE -- IT WAS TALKED ABOUT DURING THE STRATEGIC PLAN DISCUSSIONS, AND CERTAINLY IN PROP 71 ITSELF THERE'S A LOT THERE ABOUT THE CONSTITUTIONAL RIGHT TO SCNT AND SORT OF THE WANTING TO FUND THAT AMONG OTHERS BECAUSE NIH WASN'T FUNDING IT.

I THINK MY UNDERSTANDING, I DON'T DO THIS SCIENTIFICALLY, BUT MY UNDERSTANDING IS THE HOPE IS THAT DISEASE-SPECIFIC SCNT LINES WHERE THE DNA, THE SOMATIC DNA, ACTUALLY IS FROM A PATIENT WITH A SERIOUS CONDITION LIKE ALS, THE LINE THAT KEVIN EGGAN'S GROUP DERIVED, WOULD BE A MODEL FOR STUDYING THE DISEASE IN THE LABORATORY AND BY ELUCIDATING SORT OF THE PATHOGENESIS OF DISEASE WOULD POTENTIALLY OFFER NEW DRUG TARGETS, NOT NECESSARILY FOR STEM CELL RESEARCH, BUT TO FIND OTHER WAYS OF DEVELOPING POTENTIAL TESTS OR HOPEFULLY TREATMENTS FOR DISEASES.

ANYWAY, CLEARLY IT IS VERY CONCEIVABLE THAT SOMEONE WILL APPLY TO CIRM FOR FUNDING TO DERIVE A LINE THAT WOULD REQUIRE FRESH OOCYTES. AND I THINK GIVEN ALL THE CONCERNS THAT HAVE BEEN RAISED BY ADVOCACY GROUPS, BY WOMEN'S GROUPS, CERTAINLY IN LIGHT OF THE EXPERIENCE WITH THE SOUTH KOREAN SCANDAL THAT DR. HWANG'S GROUP PERPETRATED WHERE THE RISK OF OVARIAN HYPERSTIMULATION SYNDROME WAS EXCEEDINGLY HIGH, IT WAS ABOUT 20, 25 PERCENT, WE WOULD WANT, AS I THINK KEN OLDEN SAID BEFORE THE BREAK, WE WANT THIS TO BE MINIMIZED IN THIS GROUP BECAUSE THEY'RE DONATING REALLY FOR RESEARCH, NOT TO HELP THEMSELVES, NOT EVEN TO HELP ANOTHER WOMAN BEAR A CHILD. SO I THINK, AS WE ALWAYS DO IN RESEARCH, WE WANT TO MINIMIZE THOSE RISKS.

AND IT STRUCK US, US BEING ME AND ZACH HALL AND GEOFF AT CIRM, THAT THIS REPORT WAS COMMISSIONED AS A WORKSHOP, WHICH MEANS IT DOESN'T GIVE RECOMMENDATIONS. IT JUST GIVES SUMMARIES OF PRESENTATIONS FROM EXPERTS AND DISCUSSION AMONG THE PEOPLE IN THE AUDIENCE. BUT THERE IS SORT OF A -- AS WE HEARD, THERE'S NO RANDOMIZED CLINICAL TRIALS HERE OF MONITORING IN ONE WAY OR ANOTHER TO SORT OF REDUCE OHSS, BUT THERE ARE CERTAINLY EXPERIENCED CENTERS WHO HAVE TRIED TO MINIMIZE OHSS, AND THAT WISDOM, IT STRIKES ME, SHOULD BE BUILT UPON AND CONSOLIDATED. AND AS WE TRY TO LOOK IN THE LITERATURE, AND I'VE DONE ALSO AT UCSF WHERE WE DO HAVE PROTOCOLS THAT OUR SCRO COMMITTEE HAS HAD TO LOOK AT TO RECRUIT OOCYTE DONORS FOR STEM CELL RESEARCH, TRYING TO LOOK AT PUBLISHED GUIDELINES FOR MINIMIZING THE RISK OF OHSS IN THE RESEARCH SETTING. AND BECAUSE IT IS DIFFERENT THAN A CLINICAL SETTING, HOW MUCH SAFER CAN YOU BE IS THE QUESTION.

SO THIS IS A LONG KIND OF LEAD-IN TO THE IDEA THAT CIRM COMMISSIONED A GROUP OF EXPERTS IN REPRODUCTIVE SCIENCES TO REALLY ADDRESS THE QUESTION IN SOMEWHAT MORE DETAIL THAN WAS DONE FROM PAGES, WHATEVER, 54 TO THE END. WHAT GUIDELINES WOULD YOU WANT RESEARCHERS AND ALSO IRB'S OR SCRO'S THAT APPROVE

THIS RESEARCH TO THINK ABOUT AS THEY'RE EITHER DEVISING A PROTOCOL OR OVERSEEING A PROTOCOL? AND, AGAIN, THE ASSUMPTION WOULD HAVE TO BE THERE'S SCIENTIFIC MERIT, THEY'VE THOUGHT OF OTHER ALTERNATIVES, ETC., ETC.; BUT IF THERE'S A GOOD, STRONG SCIENTIFIC REASON TO USE FRESH DONOR OOCYTES, THEN WHAT SHOULD BE IN PLACE -- WHAT ISSUES NEED TO BE CONSIDERED, WHAT STEPS SHOULD BE CONSIDERED TO MINIMIZE RISKS TO OOCYTE DONORS? SO THE NOTION IS TO CONVENE AN EXPERT PANEL TO TRY TO MAKE RECOMMENDATIONS.

I THINK WHAT DO WE DO WITH THAT? I THINK THEY WOULD PRESENT TO US AS THE SWG. WE WOULD THEN, I THINK, WANT TO TAKE IT TO THE ICOC, EACH STEP OF THAT PROCESS. BOTH OUR MEETING AND THE ICOC MEETING, THERE WOULD BE AMPLE FOR TIME FOR DISCUSSION AND PUBLIC INPUT. I THINK THE STARTING POINT WOULD BE TO GET A SMALL NUMBER OF EXPERTS IN THE FIELD TO SAY HOW WOULD YOU DO IT IF YOU WERE TRYING TO MINIMIZE RISK OUTSIDE THE CLINICAL SETTING IN THE RESEARCH SETTING?

SO I WANT TO PRESENT THAT AS SORT OF WHAT MIGHT WELL BE A STEP WE WOULD WANT TO TAKE TO FOLLOW UP ON THE PREVIOUS REPORT. LET ME STOP THERE.

DR. PETERS: BERNIE, ARE YOU HAVING IN MIND THAT WOULD BE INTERNAL TO THE SWG? OR WHAT ABOUT KEN'S SUGGESTION OF ACTUALLY FUNDING IT AS A RESEARCH

PROJECT? OF COURSE, HE WAS TALKING ABOUT GATHERING DATA. HE WASN'T REALLY TALKING ABOUT RISK MINIMIZATION.

CHAIRMAN LO: WE WERE ACTUALLY THINKING OF NOT DOING IT INTERNALLY AT SWG, BUT ACTUALLY ASKING PEOPLE WHO ARE IVF ART EXPERTS WHO HAVE A LOT OF EXPERIENCE WITH IT TO SAY WHAT WOULD YOU RECOMMEND THAT WE DO? WE ALSO THOUGHT IT WOULD BE GOOD TO HAVE PEOPLE FROM OUTSIDE CALIFORNIA BECAUSE OF THE POTENTIAL THAT PEOPLE IN CALIFORNIA -- I HOPE THAT WASN'T OUR DINNER -- TO HAVE PEOPLE FROM OUTSIDE CALIFORNIA SERVE AS EXPERTS JUST TO AVOID, NOT ONLY ANY CONFLICT, EVEN THE APPEARANCE OF CONFLICT, BUT I THINK IT WOULD BE EXPERTS WHICH WE REALLY DON'T HAVE ON THE PANEL EXCEPT FOR ONE EXCEPTION THAT WE'LL TALK ABOUT IN A MINUTE; NAMELY, ROB.

DR. LOMAX: JUST TO ADD ONE OTHER COMMENT TO THAT IS THAT FROM A STANDPOINT OF ADMINISTRATIVE SORT OF SIMPLICITY AND TO MOVE FORWARD IN A SORT OF EXPEDIENT WAY, THAT THE MOST EFFICIENT MECHANISM AVAILABLE IS FOR CIRM TO COMMISSION CONSULTANTS TO MAKE RECOMMENDATIONS. AND THAT GETS THAT STEP DONE MOST EFFICIENTLY IF IT'S DEEMED TO BE THE BEST APPROACH.

CHAIRMAN LO: THE RECOMMENDATIONS WOULD BE TO THIS COMMITTEE TO THEN DELIBERATE AND DECIDE WHETHER TO

RECOMMEND TO ICOC.

DR. LOMAX: CORRECT. CERTAINLY AT THAT POINT THEN YOU WOULD WANT CERTAINLY THE BLESSING OF THIS COMMITTEE AND THEN FORWARD IT TO ICOC. I THINK THAT'S THE SPIRIT.

DR. PETERS: WHAT'S THE LEVEL OF URGENCY IF WE DID WHAT GEOFF IS SUGGESTING AND BRING IN A VARIETY OF CONSULTANTS? WOULD THAT BE QUICKER? AND IF SO, IS THAT AN ADVANTAGE?

DR. LOMAX: CERTAINLY IT'S THE MOST EXPEDIENT MECHANISM AVAILABLE TO US. I WOULD HESITATE TO COMMENT ON THE SENSE OF URGENCY BECAUSE AT THE MOMENT WE KNOW OF NO DONATION AT THIS TIME THAT'S GOING ON WITH FRESH OOCYTES FOR RESEARCH. SO THAT'S A QUESTION MARK.

CHAIRMAN LO: BUT I THINK, IF I COULD SORT OF COMMENT JUST ON TED'S QUESTION, I THINK IT WOULD BE PREFERABLE TO HAVE GUIDELINES IN PLACE BEFORE SOMEONE SUBMITS A GRANT TO US TO SAY THAT WE THOUGHT ABOUT THIS. IF YOU ARE GOING TO SUBMIT A GRANT, WE WANT YOU TO HAVE THOUGHT ABOUT IT AS WELL RATHER THAN TO SORT OF SAY, WELL, HERE'S AN INTERESTING GRANT. THEY HAVEN'T REALLY THOUGHT ABOUT THIS. SHOULD WE FUND THEM ANYWAY? THERE ARE MANY GROUPS WHO ARE TRYING TO DO THIS WITH FUNDS OTHER THAN CIRM FUNDING. SO I THINK THERE'S A LOT OF INTEREST IN DERIVING -- SO FAR, AS ONE OF THE

PUBLIC COMMENTERS SAID, THESE HAVE NOT BEEN SUCCESSFUL. THERE'S CERTAINLY A LOT OF EFFORT IN THE UK. ALISON MURDOCK AT NEWCASTLE AND IAN WILMOT ARE BOTH WORKING ON THIS. IN THE U.S. THERE ARE A NUMBER OF GROUPS, INCLUDING ACTUALLY, AGAIN DISCLOSURE, A GROUP AT UCSF TRYING TO DO THAT. I THINK ROGER PETERSON.

DR. TAYLOR: WE TRIED IN THE PAST.

CHAIRMAN LO: SO THERE'S A LOT OF INTEREST IN DOING THIS. IT'S VERY INTERESTING. A LOT OF PEOPLE HAVE SAID THAT IF THERE IS A STEM CELL LINE WITH A DISEASE I'M INTERESTED IN STUDYING, I WOULD WANT TO HAVE ACCESS TO THAT TO BE ABLE TO CARRY OUT OTHER TYPES OF STUDIES.

MR. SHEEHY: I GUESS I HAVE A COUPLE OF QUESTIONS. AND I THINK WE HAVE FUNDED ONE SCNT STUDY ALREADY. I THINK WE FUNDED RENE PARA. I THINK THAT'S THE STANFORD COMPREHENSIVE. I THINK THAT IS SCNT. WE HAVE ANOTHER THAT'S IN A GRAY AREA THAT'S USING FROZEN EGGS. I DON'T REMEMBER WHAT THE PROVENANCE WAS OF HOW SHE WAS -- I DON'T REMEMBER THE DETAILS OF HER STUDY MAINLY BECAUSE IT WAS A UCSF STUDY. I THINK WE FUNDED IT, AND THEN IT --

CHAIRMAN LO: RENE MOVED.

MR. SHEEHY: I DON'T THINK I EVER SAW IT. AND I KNOW THAT FROM THE GRANTS WORKING GROUP THAT

THERE'S A LOT OF INTEREST IN FUNDING -- THE DIRECTIVE BACK TO THE ICOC HAS BEEN OR TO CIRM HAS BEEN TO ENCOURAGE FUTURE RFA'S THAT WOULD ELICIT MORE SCNT APPLICATIONS. SO I THINK, YOU KNOW, WE HAVE KIND OF, AT LEAST FROM MY PERSPECTIVE, BECAUSE I THINK I SHARE SOME OF DR. OLDEN'S CONCERN. THIS IS GOING ON AS WE SPEAK. AND, YOU KNOW, WE'RE TALKING ABOUT GETTING MORE INFORMATION BEFORE WE PUT IN PLACE POLICIES THAT SHOULD BE IMPACTING THINGS THAT MAY BE BEFORE US BEFORE THE POLICIES ARE IN PLACE. DOES THAT MAKE SENSE?

AND I KNOW ONE OF THE MORE CONTROVERSIAL -- I HAD SUGGESTED INTERNALLY THAT WE BRING ONE OF THE MORE CONTROVERSIAL, MAINLY THE FROZEN EMBRYO, FROZEN EGG ONE, TO THIS WORKING GROUP TO REVIEW. AND I DON'T KNOW IF WE MIGHT WANT TO POTENTIALLY CONSIDER IN THIS INTERIM PERIOD MAYBE REVIEWING -- YOU KNOW, HAVING THIS GROUP, AND WE CAN MEET TELEPHONICALLY. WE WOULDN'T ALL HAVE TO COME TOGETHER, BUT MAYBE HAVING A REVIEW. MY COMFORT LEVEL -- THE FROZEN EGG ONE HAD NOT EVEN BEEN TO A SCRO. A SCRO HAD NOT BEEN SET UP TO REVIEW IT, AND WE'D ALREADY APPROVED THE FUNDS.

I JUST DON'T -- THIS IS THE ONE AREA OF THE WHOLE ENTERPRISE THAT I HAVEN'T EVER FOUND MY FEET ON PERSONALLY. AND I DON'T KNOW IF THAT'S OF INTEREST HERE TO MAYBE HAVE A LOOK AT THOSE. I'M NOT SENSING

THAT THERE'S THOUSANDS OF THEM COMING ACROSS, BUT THE WAY WE'RE SET UP NOW IS IF THE UNIVERSITY HAS A SCRO, THE SCRO LOOKS AT IT THAT'S CERTIFIED, BUT I JUST HAVEN'T -- MY GUT FEELS A LITTLE UNEASY ABOUT THESE EGG ISSUES AND WHETHER WE'RE REALLY GETTING AN APPROPRIATE LEVEL OF SCRUTINY BEFORE WE FUND THESE. I'M JUST PUTTING THAT OUT THERE. I DON'T HAVE A SPECIFIC SUGGESTION.

AND I AGREE WITH GOING FORWARD AND COLLECTING MORE DATA AS EXPEDITIOUSLY AS POSSIBLE, BUT I FEEL THAT PROBABLY BEFORE THE END OF THIS YEAR WE WILL BE FUNDING SCNT GRANTS. I'M ALMOST CERTAIN THAT WILL BE TRUE.

CHAIRMAN LO: WELL, AGAIN, LET ME SORT OF JUST TRY AND MAKE A CLARIFYING COMMENT, JEFF. I THINK YOU'RE WANTING TO FEEL ETHICALLY SECURE ABOUT ANY SCNT RESEARCH THAT CIRM FUNDS, I THINK, IS SOMETHING THAT HAS -- MANY PEOPLE CERTAINLY HOLD THAT AS AN ASPIRATION. WHAT I WAS TALKING ABOUT, WHICH I THINK IS DIFFERENT FROM WHAT KEN OLDEN WAS TALKING ABOUT EARLIER, WAS SUGGESTING NOT COLLECTING DATA, BUT ACTUALLY JUST GOING AND TRYING TO GET THE BEST THINKING OF PEOPLE WHO DO A LOT OF CLINICAL ART AND SAYING, IF WE WANT TO MINIMIZE THE RISK OF OHSS IN OOCYTE DONORS, WHAT WOULD YOU ALL SUGGEST BE SORT OF THE GUIDELINES, THE RULES OF THUMB, THE ISSUES THAT PEOPLE SHOULD BE

CONSIDERING? AND LET US PUT THAT IN PLACE TO HELP, I GUESS, THE APPLICANTS WHO ARE PRESENTING PROTOCOLS, THE SCRO'S AND IRB'S THAT REVIEW THEM, AND POTENTIALLY ALSO THE CIRM.

IT STRIKES ME WE WOULD WANT TO MAKE SURE THAT ANYTHING THAT WE WERE FUNDING WOULD HAVE ADDRESSED ALL THOSE POINTS. AND, AGAIN, MY SENSE IS THAT THERE'S A LOT OF GOOD THINKING OUT THERE, BUT PEOPLE ARE DOING IT IN -- THEY HAVEN'T BROUGHT DIFFERENT CENTERS TOGETHER AND SAID LET'S SORT OF GET THE BEST OF THE BEST.

DR. ROWLEY: I THINK I WOULD CERTAINLY SUPPORT THAT BECAUSE MANY DIFFERENT GROUPS AND STATES ARE STRUGGLING WITH A NUMBER OF THESE ISSUES. AND I THINK ONE OF THE GOOD THINGS ABOUT THE NATIONAL ACADEMY REPORT INITIALLY AND THE CLARIFICATION OF SOME OF THE GUIDELINES HAS BEEN THAT AT LEAST THERE IS SOMETHING OUT THERE FOR PEOPLE TO LOOK AT AND DECIDE DO WE AGREE. DOES IT FIT WHAT WE NEED OR NOT. AND IF CIRM CAME UP WITH SOME GUIDELINES, I'M SURE THAT THEY WOULD BE INCORPORATED OR AT LEAST CONSIDERED VERY STRONGLY AND CAREFULLY BY OTHER GROUPS FACING THE SAME PROBLEM OR WHO ALREADY ARE FURTHER DOWN THE LINE THAN CIRM IS.

MS. KING: I'M STILL TRYING TO WORK IT OUT IN MY HEAD, BUT IT GOES SOMETHING LIKE THIS. I UNDERSTAND WHY YOU'RE MAKING YOUR PROPOSAL, BERNIE, AND PART OF ME

THINKS IT'S A GOOD IDEA TO AT LEAST TRY TO CAPTURE BEST PRACTICES FROM PEOPLE WHO HAVE BEEN WORKING IN THIS AREA ALL ALONG, THE CLINICIANS. WHAT I FIND TROUBLING IS CAPTURING -- I'M TRYING TO PUT IT TOGETHER -- CAPTURING BEST PRACTICES AT THIS TIME MEANS THAT WE MOVE FULL FORCE INTO THE CLINICAL AREA WITHOUT HAVING DEALT WITH SOME OF THE DEFICIENCIES IN THE RESEARCH AS IT EXISTS.

AND SO WHAT I'M TRYING -- AND YOU KNOW ME, BERNIE, WELL TO KNOW THAT THE BIGGEST DEFICIENCY -- I MEAN THERE ARE LOTS OF DEFICIENCIES, BUT THE ONE THAT I'M MOST INTERESTED IN IS THAT WHAT WE KNOW COMES BASICALLY FROM UPPER INCOME WOMEN, NOT LOWER INCOME WOMEN AND CERTAINLY NOT RACIALLY AND ETHNICALLY DIVERSE WOMEN. AND I'VE BEEN AROUND LONG ENOUGH NOW WITH THE GRAY HAIR TO SEE THAT WHEN YOU MOVE INTO THE CLINICAL ARENA ON THAT KIND OF BASE, YOU NEVER COME OUT OF IT. AND THERE'S A CERTAIN KIND OF PROBLEM. THAT'S WHY YOU SEE MY PUZZLEMENT BECAUSE I DON'T OBJECT TO WHAT YOU'RE SAYING.

I'M TRYING TO LOOK FOR AN OPPORTUNITY BECAUSE WHAT RESEARCH WE HAVE DOESN'T APPLY TO ALL POTENTIAL DONORS. THERE ARE CLINICAL IMPLICATIONS OF THAT IN TERMS OF HOW YOU GOT INFORMED CONSENT, HOW YOU TRY TO DO YOUR RECRUITING, AND WHY YOU TRY TO DO YOUR

RECRUITING. BUT IT ALSO LEAVES ME WITH THAT DILEMMA, WHICH MAYBE IS A SECOND ISSUE, ABOUT IF WE HAVE TO ACTUALLY USE DONORS FOR LONGER PERIODS THAN WE THINK -- THAN WE'RE CURRENTLY ANTICIPATING, THAT MAYBE THERE'S SOMETHING THAT SHOULD BE DONE WITH RESPECT TO CAPTURING MORE DATA ABOUT WHAT PRACTICES ARE.

I DON'T KNOW IF THAT HELPS, BUT THAT IS MY BEWILDERMENT BECAUSE --

CHAIRMAN LO: LET ME PUSH A LITTLE BEYOND THAT BECAUSE IT STRIKES ME, IF I TRY AND TAKE ANOTHER STEP DOWN WHAT YOU SAID, AND I GUESS I WOULD TIE IT BACK TO WHAT KEN OLDEN SAID, SORT OF WANTING TO HAVE THE POOL OF OOCYTE DONORS FOR RESEARCH TO SOME EXTENT BE REPRESENTATIVE OF THE POPULATION AS A WHOLE. AND THERE ARE SCIENTIFIC REASONS FOR WANTING TO DO THAT AS WELL.

MS. KING: RIGHT.

CHAIRMAN LO: PAT, IF I COULD SORT OF TAKE A COUPLE STEPS BEYOND WHAT YOU WERE SAYING, IN THAT INFORMED CONSENT PROCESS, IF I'M TALKING TO A WOMAN OF COLOR TO WHOM THE CURRENT DATA ON RISK MAY NOT APPLY FOR A NUMBER OF REASONS, WE'RE TRYING TO SAY IT WOULD BE A GOOD THING TO HAVE MORE OOCYTES FROM PEOPLE LIKE YOU. ON THE OTHER HAND, IN ALL HONESTY, WE'D HAVE TO SAY ALL THE DATA WE KNOW ABOUT RISK IS NOT FROM WOMEN

LIKE YOU. WE WILL DO ALL THE THINGS WE CAN DO TO MINIMIZE RISK, AND WE THINK THAT IT SHOULD MINIMIZE RISK FOR YOU ALTHOUGH IT'S NEVER BEEN TRIED IN PEOPLE LIKE YOU. THAT STRIKES ME AS A VERY COMPLEX DISCUSSION TO HAVE, BUT IT WOULD BE VERY IMPORTANT FOR THE REASONS YOU SAID AND THE REASONS KEN OLDEN SAID.

MS. KING: THANK YOU, BERNIE. AS ALWAYS, YOU DO ME BETTER THAN I DO MYSELF. AND WE WORKED TOGETHER FOR A LONG TIME. THAT IS EXACTLY THE DILEMMA THAT I SEE, BUT I THINK THAT THE REASONS FOR THE POOL BEING REPRESENTATIVE ARE REALLY CRITICAL. AND SO THAT MEANS THAT WE CAN'T SORT OF CAPTURE BEST PRACTICES. WHAT WE REALLY NEED TO DO IS TO THINK THROUGH THE IMPLICATIONS OF WHAT ARE EXISTING PRACTICES, IF YOU FOLLOW YOUR ROUTE, AND HOW WE MIGHT NEED TO THINK HARD IN SOME AREAS TO HELP US DEAL WITH WHAT I SEE AS A REALLY TOUGH COMPLEX PROBLEM.

A SEPARATE ISSUE IS HOW YOU GET BETTER DATA, BUT I'LL PUT THAT TO ONE SIDE. THAT'S WHY I WAS SITTING HERE LOOKING PUZZLED.

DR. TAYLOR: I GUESS JUST A COUPLE OF COMMENTS. I COMPLETELY AGREE WITH WHAT PAT SAYS. AND HER FINAL QUESTION, HOW DO WE GET BETTER DATA, IS REALLY A CRITICAL ONE. AND I THINK THIS IS THE ONE THAT KEN IS RAISING TOO. SCIENTIFICALLY IT CERTAINLY

HAS BEEN MY HABIT TO WANT TO HAVE AS MUCH INFORMATION AS YOU CAN HAVE BEFORE GOING FORWARD, BUT WE DO PROBABLY HAVE A BIT OF A PRAGMATIC ISSUE HERE WHERE SCNT PROTOCOLS WILL BE COMING THROUGH. THERE ARE GOING TO BE PROTOCOLS CERTAINLY ADDRESSING SOME OF THE ISSUES ABOUT SAFETY COMING FROM DIFFERENT INSTITUTIONS. THEY MAY BE KIND OF INFORMATIVE IN THE WAY THEY'VE KIND OF CONSTRUCTED THE LITTLE BITS OF DATA THAT ARE OUT THERE, AND IT COULD BE INTERESTING TO US.

BUT THE THING THAT I FEAR IS THAT WE REALLY HAVE VERY, VERY LIMITED ACCESS TO GOOD INFORMATION, AND I DON'T FORESEE THAT IT'S GOING TO BE DRAMATICALLY ENHANCED OVER THE NEXT COUPLE OF YEARS JUST BECAUSE OF THE PRIVACY ISSUES AROUND DONATION CANDIDATES AND REALLY THE FRAGMENTED WAY THAT WE ACTUALLY KIND OF RECORD THESE DATA, PARTICULARLY IN THIS COUNTRY, IF WE RECORD IT AT ALL. SO IT'S A LITTLE BIT OF A BALANCING ACT, I THINK.

IT WOULD BE NICE TO COME UP WITH SOME BEST PRACTICES BASED ON THE PRAGMATISM OF THE MOST EXPERIENCED PEOPLE, MAYBE UNDERSTANDING LIMITATIONS THAT IT'S QUITE NONREPRESENTATIVE BECAUSE TYPICALLY THE COUPLES SEEKING DONOR OOCYTES ARE OF A PARTICULAR SOCIOECONOMIC, ETHNIC SORT OF SLICE OF THE POPULATION, AND THEY'RE LOOKING FOR DONORS THAT SORT OF MATCH THOSE

CHARACTERISTICS. AND I DO ANTICIPATE THAT THERE ARE GOING TO BE SIGNIFICANT DIFFERENCES. I THINK GENETIC DIFFERENCES IN PRETERM LABOR, FOR EXAMPLE. WE KNOW THAT THERE ARE TNF ALPHA PROMOTER POLYMORPHISMS THAT PROBABLY PREDISPOSE AFRICAN AMERICAN WOMEN TO PRETERM LABOR MORE THAN CAUCASIAN WOMEN. THOSE PRO-INFLAMMATORY SORT OF GENE SORT OF GENETIC POLYMORPHISMS MIGHT WELL PREDISPOSE TO MORE INFLAMMATION AND A GREATER RISK FOR OOCYTE RETRIEVAL AS WELL.

SO I THINK THAT DR. GUIDICE DID A NICE JOB PRESENTING THE RISK OF INFECTION AND INFLAMMATION, AT LEAST THAT WE PICK UP CLINICALLY, SEEMS TO BE REALLY QUITE LOW IN THIS POPULATION IN SORT OF THE PREDOMINANTLY WHITE POPULATION THAT'S BEEN STUDIED. WE HONESTLY DON'T KNOW WHAT THAT'S GOING TO TRANSLATE TO. I THINK ONE COULD ANTICIPATE SOME CHANGES, BUT WE MAY NOT BE ABLE TO WAIT FOR THE DATA TO KIND OF COME IN AND BE COMFORTABLE WITH IT AND ADDRESS SOME OF THE QUESTIONS THAT JEFF HAS RAISED ABOUT THE PROTOCOLS AS THEY SORT OF FLIP FORWARD. IT IS A PUZZLING SITUATION. YOU'RE RIGHT TO BE PUZZLED.

DR. ROWLEY: I JUST WANTED TO FOLLOW ON WITH WHAT YOU'VE SAID AND ASK YOU A COUPLE OF QUESTIONS, WHICH YOU'VE PARTLY ANSWERED. AND THEY HAVE TO DO WITH

WHAT YOU EXPECT, BASED ON YOUR EXPERIENCE, TO BE DIFFERENCES IN, SAY, CAUCASIANS VERSUS AFRICAN AMERICANS VERSUS HISPANICS IN THE AREA THAT WE'RE CONCERNED ABOUT RIGHT HERE.

DR. TAYLOR: I'LL ADMIT THAT THAT EXAMPLE MIGHT BE A BIT OF A STRETCH. I'M JUST KIND OF TRYING TO UNDERSTAND AT LEAST SOME OF THE COMPLEXITIES OF THINGS THAT I KNOW ABOUT IN A KIND OF BROADER REPRODUCTIVE MEDICINE SCOPE.

I DO THINK THAT IF WE GOT TOGETHER EXPERTS WITH THE MOST EXPERIENCE IN THE DONOR CYCLE SETTING WHERE THEY REALLY ARE NOT -- SO THERE'S SOME DIFFERENCES THERE CLEARLY. IT TENDS TO BE A YOUNGER POPULATION, WOMEN WHO HAVE FAIRLY SENSITIVE OVARIAN RESPONSES, SO THEY GENERALLY REQUIRE LESS MEDICATION.

DR. ROWLEY: NOW, YOU TALKING ABOUT ONE GROUP ETHNICALLY COMPARED WITH ANOTHER?

DR. TAYLOR: I'M JUST REALLY SORT OF TALKING ABOUT THE EXPERIENCE THAT WE HAVE. NO. IF WE THINK ABOUT -- AND, AGAIN, SO WE MAY WANT -- I GUESS IF WE WANTED TO IDENTIFY A REALLY LOW RISK GROUP FOR OVARIAN HYPERSTIMULATION SYNDROME, WHICH IS GOING TO BE THE MOST SIGNIFICANT AND COMMON COMPLICATION THAT WE COULD POSSIBLY DEAL WITH? BASED ON THE EXPERIENCE THAT WE HAVE WITH OUR DONORS FOR REPRODUCTIVE PURPOSES, I THINK

THAT IT WOULD BE FEASIBLE TO COME UP WITH BEST PRACTICES THAT PERTAIN TO THAT PARTICULAR POPULATION, AND THEN TO TRY TO NOODLE OUT SOME OF THE THINGS, BUT IT WOULD BE MORE OF A SUPRATENTORIAL TYPE OF PROCESS RATHER THAN ONE THAT WOULD BE BASED ON DATA, I'M AFRAID.

CHAIRMAN LO: I'VE HEARD THREE DIFFERENT ISSUES THAT SEEM TO ME QUITE IMPORTANT. ONE IS THE POINT THAT A NUMBER HAVE RAISED. I THINK KEN OLDEN RAISED IT FIRST. WE NEED MORE DATA, BETTER DATA ON RISKS TO OOCYTE DONORS. SECOND IS JEFF SHEEHY'S CONCERN THAT THERE WILL BE PROTOCOLS BEING SUBMITTED TO CIRM THAT MAY SCIENTIFICALLY HAVE SCORES THAT ARE FUNDABLE, BUT WHERE THE SCRUTINY TO THE ETHICS OF OOCYTE DONATION MAY NOT BE AS CAREFULLY BUILT INTO THE CURRENT CIRM REVIEW SYSTEM WHERE WE'RE SORT OF DEFERRING TO SOME EXTENT TO SCRO'S. THIRD QUESTION IS THE ONE I HAD RAISED ABOUT, EVEN KEEPING IN MIND ALL THE LIMITATIONS OF THE DATA THAT A NUMBER OF US HAVE COMMENTED ON, WOULD THERE BE MERIT IN CALLING FOR EXPERT CONSULTANTS TO SORT OF SUGGEST BEST PRACTICE GUIDELINES.

SO THERE'S THREE VERY DIFFERENT SORT OF PARTS OF THIS CONCERN WE ALL HAVE OF SORT OF TRYING TO PROTECT WOMEN WHO DONATE OOCYTES FOR RESEARCH.

DR. PETERS: I'M THINKING, BERNIE, EARLIER YOU HAD SAID MAYBE OUR GRANTEES OUGHT TO KNOW WE HAD THOUGHT ABOUT THIS. WELL, WE'VE ACTUALLY BEGUN TO THINK ABOUT IT TODAY. AND LINDA'S REPORT GAVE US CERTAINLY A POINT OF DEPARTURE. SO I WONDER IF WE'VE GOT TWO OVERLAPPING ISSUES. ONE IS, YES, RESEARCHERS PROCURING FRESH EGGS OUGHT TO, ON THE BASIS OF WHATEVER THEIR CRITERIA ARE, TO MINIMIZE RISK IN THAT PROCESS. AND IT WOULD BE NICE IF WE COULD PROVIDE SOME STANDARDS FOR MINIMIZATION OF RISK. WE'RE PROBABLY NOT READY TO GIVE A COMPREHENSIVE SET OF STANDARDS, BUT WE PROBABLY COULD DO SOME.

THEN OVER A LONGER HAUL, THE SECOND RELATED ISSUE IS HOW DO SOCIAL AND ECONOMIC AND DIETARY AND RACIAL FACTORS REFINE WHAT THESE RISKS COULD BE. WE'VE ALREADY HAD SOME EXPERIENCE WITH SOME INTERIM GUIDELINES, AND WOULD IT BE OUT OF ORDER TO PERHAPS PROCEED WITH WHAT YOU AND GEOFF HAVE BEEN -- GEOFF LOMAX HAVE BEEN SUGGESTING, TO ENGAGE IN OBTAINING BEST PRACTICE INFORMATION, PROVIDE SOME KIND OF INTERIM GUIDELINES WHICH WOULD MAKE ONE POINT. IT'S UP TO YOU AS A RESEARCHER, IF YOU GOT CIRM MONEY, TO MINIMIZE THE RISKS FOR THESE PEOPLE. AND THEN HAVE THAT STAND FOR A PERIOD OF TIME WHILE WE REFINE WHAT THAT WOULD LOOK LIKE. THAT WOULD MEET, I THINK, SOME OF JEFF SHEEHY'S

CONCERNS HERE ABOUT INCOMING APPLICATIONS.

CHAIRMAN LO: AGAIN, THERE'S SORT OF REGULATORY ISSUES HERE. AND I THINK THAT YOU USE THE TERM "GUIDELINES," TED, WHICH I THINK IS THE RIGHT TERM WE SHOULD BE THINKING IN. THESE ARE NOT REGULATIONS. I THINK WE'RE -- THESE ARE THINGS WE REALLY WANT PEOPLE TO THINK ABOUT; AND IF THEY DISAGREE, THEY MIGHT WELL HAVE GOOD REASONS, BUT THEY NEED TO HAVE THOUGHT IT THROUGH AND BE READY TO EXPLAIN WHY THEY THINK IN THEIR CASE THE GUIDELINES DON'T NECESSARILY APPLY. SO THEY WOULD BE MORE FLEXIBLE THAN REGULATIONS, BUT THEY WOULD HAVE A LOT OF SORT OF AUTHORITY.

I THINK, AS TED POINTS OUT, PROBABLY ONE OF THE IMPORTANT THINGS MAY BE TO SAY, LOOK. WE REALLY THINK THIS IS IMPORTANT, AND YOU HAVE AN ETHICAL DUTY TO MINIMIZE RISKS, AS YOU DO IN ALL HUMAN PARTICIPANTS RESEARCH, BUT HERE IN PARTICULAR IT'S ESPECIALLY IMPORTANT AND IT'S ESPECIALLY COMPLICATED.

AND SO, YOU KNOW, I GUESS TO GO BACK TO JEFF'S POINT, THE HOPE MIGHT BE THAT BEFORE SUBMITTING A GRANT, THE RESEARCHER WHO WANTS TO TRY TO DERIVE AN SCNT LINE WILL HAVE READ THROUGH, APPLIED, THOUGHT ABOUT, AND INCORPORATED GUIDELINES THAT AN EXPERT PANEL MIGHT PRODUCE. THAT STILL STRIKES ME THIS OTHER PIECE OF GETTING MORE DATA FOR THE FUTURE AND DOING IT IN A

WAY THAT'S EFFICIENT.

MS. KING: I WAS GOING TO SAY I DON'T THINK ANYBODY IS GOING TO BE AGAINST GUIDELINES, BUT THERE SEEMS -- I DON'T, SO THE QUESTION IS CAN WE TAKE CARE OF OR TRY TO GET TO SOME OF THE OTHER ISSUES.

MY VIEW ABOUT GUIDELINES AND USING AN EXPERT PANEL TO HELP YOU DO THAT IS THAT WE SHOULD HAVE AN EYE TOWARDS WHO WE SELECT FOR THE EXPERT PANEL, NOT JUST EXPERTISE, BUT PEOPLE WHO WORK IN CERTAIN KINDS OF AREAS. IT IS NOT THE CASE THAT AFRICAN AMERICANS AND OTHER ETHNIC GROUPS DO NOT USE REPRODUCTIVE TECHNOLOGIES. THEY DO. THEY TEND TO BE HIGH INCOME TOO. AND THE QUESTION IS IS THERE ANY WAY THAT WE CAN CATCH, NOT THE CAREFULLY CONDUCTED STUDIES, BUT WHETHER WE CAN AT LEAST GET SOME OF THE EXPERIENCE WHERE IT IS AVAILABLE. SO WE COULD -- I WOULD THINK THAT WOULD BE CRITICAL ALONG WITH THE EXPERTISE THAT YOU NEED. I DON'T THINK YOU SHOULD HAVE ANY TROUBLE DOING IT AS LONG AS WE THINK ABOUT IT IN ADVANCE AND SELECT FROM CERTAIN PARTS OF THE COUNTRY AND CERTAIN REGIONS OF THE COUNTRY, NOT JUST FOR AFRICAN AMERICANS HERE, BUT FOR ALL THE RACIAL AND ETHNIC MINORITIES. THERE ARE CERTAIN PLACES WHERE YOU CAN GO WHERE YOU WILL FIND A GREATER IMPACT FROM CERTAIN GROUPS.

JEFF'S ISSUE IS MORE INTERESTING BECAUSE I'VE

ALWAYS THOUGHT THAT YOU LEARN A GREAT DEAL WHEN YOU SEE AN ACTUAL APPLICATION IN AN AREA THAT'S TROUBLING TO YOU. SO I DON'T KNOW HOW THIS WORKS IN CALIFORNIA, OR HOW IT COULD WORK OR WHETHER IT'S JUST FOR OUR EDUCATION AND NOT FOR REVIEW AND TELLING PEOPLE WHAT TO DO, BUT WE SHOULDN'T LOSE THE THOUGHT THAT SEEING SOME OF THE EARLY APPLICATIONS ABOUT SCNT AND THESE ISSUES OF WHAT THE RESEARCHERS HAVE PROPOSED TO DO COULD BE INSTRUCTIVE. I'M TRYING TO CHOOSE MY WORDS CAREFULLY. I'M NOT SUGGESTING WE PASS ON THEM, TURN THEM DOWN. I'M NOT SURE THAT'S APPROPRIATE EVEN, BUT THEY CERTAINLY WOULD BE INSTRUCTIVE BECAUSE YOU WOULD GET A REAL SENSE OF HOW PEOPLE ON THE GROUND ARE WORKING AND WHAT THEY'RE THINKING AND WHAT THEY SEE AS ISSUES. AND SO I DON'T WANT TO LOSE JEFF'S THOUGHT. I JUST DON'T KNOW HOW TO IMPLEMENT IT.

I CERTAINLY THINK SOMETHING CAN BE GAINED IN THIS EARLY PERIOD IF YOU JUST TAKE A LOOK AT THE FIRST TEN, 15 THAT COME THROUGH OVER THE NEXT YEAR AND A HALF. THERE'S A CERTAIN KIND OF KNOWLEDGE THAT YOU CAN JUST GET FROM THAT AND A CERTAIN UNIFORMITY OF APPROACH THAT'S DESIRABLE THAT MIGHT COME OUT OF THAT. A MUCH MORE UNIFORM TAKE WOULD BE POSSIBLE.

DR. LOMAX: COULD I OFFER, BERNIE, JUST TWO POINTS TO INJECT IN THE DELIBERATION? ONE WAS JUST THE

GENESIS OF THE GUIDELINES CONCEPT WAS BASED ON A LIMITED, BUT SOME DISCUSSION SURVEYING AROUND TO INSTITUTIONS. AND THE AUDIENCE THAT THIS SEEMED MOST USEFUL FOR WAS GIVING IRB'S -- I THINK THE TERM "BENCHMARKS" CAME INTO THE DISCUSSION -- THAT IRB'S ARE FEELING A LITTLE BIT IN AN AREA, OR AT LEAST IN THE INSTITUTIONS REPRESENTED, IN THE THREE OR FOUR INSTITUTIONS, THAT THESE WILL BE USEFUL BENCHMARKS. I JUST INSERT THAT JUST TO SORT OF SAY, JUST TO AMPLIFY AN AUDIENCE AND WHERE THAT CAME FROM.

THE OTHER POINT ON NEW DATA, AND THIS WAS, I THINK, REALLY CERTAINLY WHAT DR. HALL ENVISIONED, AND I HESITATE TO SPEAK FOR HIM, BUT IT'S SORT OF IN THIS UNUSUAL AREA WHERE IT'S KIND OF THE ORGANIZATIONAL DILEMMA OF BUDGET BUREAUCRACIES. BUT WITHIN THE STRATEGIC PLAN THERE IS A SOCIETAL ISSUES PROGRAM THAT IS REALLY THERE'S A COMMITMENT OF FUNDING THERE, I THINK. AND MY UNDERSTANDING WITH DR. HALL WAS THAT HE SORT OF SAW THAT AS THE OPPORTUNITY FOR THE NEW DATA GENERATION AND THE NEW RESEARCH. AND SO IT'S A BIT OF A DILEMMA; THEREFORE, WE DON'T APPROACH IT HOLISTICALLY. WE'RE SORT OF APPROACHING IT FROM A DIFFERENT PIECE OF OUR BUDGET AND HOW WE FUND THINGS AND HOW WE GO ABOUT DOING THINGS.

BUT CERTAINLY I JUST WANT TO POINT OUT THAT I

THINK THE VISION FOR THE DATA GENERATION IS THERE, AND IT'S REFLECTED IN THE STRATEGIC PLAN, BUT I THINK WHAT I SENSE FROM THE COMMENTS HERE IS IT LACKS A LITTLE BIT OF THAT HOLISTIC QUALITY THAT IS EMERGING IN THIS CONVERSATION, JUST TO POINT THAT THAT PIECE OF THE STRATEGIC PLAN IS INTEGRAL TO CIRM MOVING FORWARD.

CHAIRMAN LO: GEOFF, CAN I ASK YOU. THE STRATEGIC PLAN ALSO HAS A TIMELINE. IS THERE A SENSE OF WHEN IN THE LIFE OF CIRM THIS KIND OF RESEARCH MIGHT BE PRIORITIZED BECAUSE WE'VE DONE TRAINING GRANTS, WE'RE GOING THROUGH A CYCLE OF SEED GRANTS?

DR. LOMAX: I THINK THAT'S A QUESTION I'D HAVE TO BRING BACK TO THE FOLKS. OR PERHAPS JEFF, HE'S HAD MORE EXPERIENCE.

MR. SHEEHY: I THINK IT'S DOWN THE ROAD. AND I JUST -- I GET MORE AND MORE OF A SENSE THAT THE REAL URGENCY FOR SCNT AND EGG DONATIONS IS AT THE FRONT END, AND THAT'S MORE RETROSPECTIVE. AND, YOU KNOW, THERE'S A LOT MORE FLEXIBILITY IN WHAT WE CAN DO WITHIN THE CONSTRUCT OF THIS COMMITTEE. IT'S REALLY UP TO US. WE HAVE A FAIRLY BROAD MANDATE, BUT WE ALSO HAVE A FAIRLY BROAD RESPONSIBILITY.

AND JUST TO TALK TO DR. KING'S POINT, HAVING SAT IN THROUGH A NUMBER OF GRANTS WORKING GROUP SESSIONS, THERE IS KIND OF A COLLECTIVE KNOWLEDGE BASE

THAT GETS CREATED HAVING REVIEWED SEVERAL APPLICATIONS THAT GIVES YOU A TEXTURE AND A SENSE OF WHAT'S GOING ON AND A SENSIBILITY. THIS IS NOVEL FOR EVERYBODY, I THINK. I THINK IT'S NOVEL FOR THE INSTITUTIONS. I THINK IT'S NOVEL FOR THE RESEARCHERS. IT'S NOVEL FOR US. AND WE CAN AFFORD TO BE CREATIVE IF THAT'S OUR DESIRE.

AND I WOULD NOTE THAT THERE ALWAYS SEEMS TO BE A PRESUMPTION THAT WE'RE ALWAYS GOING TO BE TALKING ABOUT STANFORD, UCSF, AND UCLA, JUST TO THROW OUT, YOU KNOW, PRISTINE INSTITUTIONS WITH PRISTINE REPUTATIONS THAT WILL ALWAYS DO THE RIGHT THING IF GIVEN -- PRESUMABLY. WELL, THE PRESUMPTION. BUT WE'RE PRESUMING THAT WE'RE ALWAYS GOING TO BE DEALING WITH GOOD ACTORS, AND THERE'S A MAJOR IMPETUS IN, YOU KNOW, FOR A WHOLE HOST OF REASONS, NOT THE LEAST OF WHICH THAT THEY MAKE THERAPIES TO INVOLVE THE PRIVATE SECTOR. AND HOW DO WE START TO REALLY GET A GRIP ON ALL OF THIS?

YOU KNOW, THIS FRONT-END PORTION, WHICH IS THE SLIPPERIEST AND THE MOST DIFFICULT TO GET THE HANDLE ON, IS ALSO PROBABLY THE MOST CRITICAL. WE SUFFER FROM A SURFEIT OF INFORMATION AND DATA, BUT, YOU KNOW, WE CAN ACTUALLY GIVE SOME FAIRLY CLEAR DIRECTION. FOR INSTANCE, THERE IS A POT OF MONEY THAT'S

UNALLOCATED SO FAR FROM OUR VARIOUS GRANT ROUNDS. WE HAVEN'T COMPLETELY SPENT EVERY DIME, UNLESS LORI HOFFMAN HAS LEFT, BUT I THINK -- WE COULD DIRECT FROM THIS MEETING AS PART OF THE REPORT THAT GOES TO THE ICOC THAT SOME OF THE DATA COLLECTION EFFORTS, YOU KNOW, BE PUSHED FORWARD AND THAT THIS TAKE PLACE NOW. AND IF WE MAKE SOME OF THE APPROVAL FOR -- IF WE CAN TIE THAT TO FUNDING SCNT GRANTS, WHICH IS A PRIMARY SCIENTIFIC EFFORT, YOU KNOW, THESE ARE NOT UNRELATED, SEPARATE, DISCRETE ENTITIES. THESE ARE ALL RELATED, AND THEY CAN HAPPEN AT THE SAME TIME.

ONE OF OUR BIGGEST BURDENS IS THAT OUR STAFF HAS BEEN SMALL BECAUSE OUR STAFF IS FUNDED THROUGH A PERCENTAGE OF THE GRANTS THAT WE GIVE OUT. BUT AS WE START TO GIVE OUT MORE GRANTS, AND WE WILL HAVE A NEW PRESIDENT, BY THE WAY, IN JUNE, I FEEL CERTAIN, HAVING SEEN THE SHORT LIST OF THE PEOPLE THAT WE PLAN TO INTERVIEW, THAT THERE IS CERTAINLY TALENT THERE. SO I THINK THAT THIS WILL ALL GO, BUT WE NEED TO FIGURE OUT OUR ROLE IN THIS GREATER PIECE AND HOW MUCH OF A ROLE WE WANT TO PLAY, I GUESS, JUST TO PUT THAT OUT THERE. BUT THE RESOURCES, I THINK, ARE AVAILABLE.

CHAIRMAN LO: SO LET ME AGAIN -- I THINK THIS HAS BEEN VERY USEFUL. LET ME TRY AND SEE IF I'VE HEARD RIGHT WHAT PEOPLE ARE SAYING. IT SOUNDS LIKE THAT I'VE

NOT HEARD ANYONE SAY THIS NOTION OF CONVENING A GROUP OF EXPERTS TO MAKE RECOMMENDATIONS FOR BEST PRACTICE GUIDELINES IS A BAD IDEA. THERE HAVE BEEN SOME HELPFUL SUGGESTIONS THAT THE MEMBERS OF THAT PANEL HAVE EXPERIENCE WITH AND INTEREST IN THE PARTICULAR WAYS IN WHICH WOMEN WHO ARE NOT WELL REPRESENTED IN THE DATA WE NOW HAVE MIGHT BE AT DIFFERENT KINDS OF RISK AND TO DRAW ON CLINIC EXPERIENCE IN THE ABSENCE OF DATA.

BUT I'VE ALSO HEARD THAT THAT'S SORT OF GOOD, BUT NOT THE WHOLE PICTURE, AND THERE ARE TWO OTHER IMPORTANT PARTS I'VE HEARD. ONE IS THAT WE NEED TO KIND OF TRY AND GET BETTER DATA, MORE POPULATION SORT OF REPRESENTATIVE DATA ON THE RISK TO OOCYTE DONORS. OUR MANDATE WOULD BE FOR RESEARCH. WE CAN'T DO ALL OF IVF.

THEN ALSO JEFF SHEEHY'S POINT THAT AS GRANTS ARE BEING SUBMITTED TO CIRM, WHAT ROLE MIGHT THIS GROUP PLAY IN THAT PROCESS? I'VE HEARD SEVERAL VERY DIFFERENT SORT OF SUGGESTIONS. ONE, WHICH I WILL ASCRIBE TO JEFF, IS THAT THIS MAY ACTUALLY BE OF USE IN THE REVIEW PROCESS AND HELP CIRM AS AN ORGANIZATION SORT OF AVOID FUNDING RESEARCH THAT'S SCIENTIFICALLY VERY STRONG, BUT ETHICALLY LESS STRONG. I MAY HAVE EXAGGERATED.

MR. SHEEHY: I THINK IT'S MORE DYNAMIC THAN

THAT. I THINK IT'S LESS ABOUT THUMBS UP, THUMBS DOWN. IT'S MORE LIKE IF YOU DO XYZ --

CHAIRMAN LO: YOU COULD BE BETTER.

MR. SHEEHY: THIS WOULD BE APPROPRIATE AS OPPOSED TO THE WAY THAT YOU'RE PLANNING, EITHER FROM EXPERIENCE OR FROM AN ETHICAL VIEWPOINT, WE FIND IT TROUBLING.

CHAIRMAN LO: SO IT'S MORE OF A QUALITY IMPROVEMENT CONSULTANT.

MR. SHEEHY: IN THE SAME WAY THAT THE SCIENTISTS CAN LOOK AT A STUDY AND SAY, YOU KNOW, IF YOU JUST HAD SUBMITTED IT AS X, THIS WOULD BE A GREAT STUDY, BUT THEY SUBMITTED Y. AND THEY'RE FIGHTING IN THE GRANTS WORKING GROUP ACTUALLY TO GET INTO A MORE DYNAMIC SITUATION WHERE IT'S NOT THUMBS UP, THUMBS DOWN TYPICAL OF NIH, BUT MORE LIKE GETTING FEEDBACK AND THEN GETTING IMPROVEMENT. AND I THINK, GIVEN THE TIMELINES THAT WE'RE TRYING TO WORK ON, FROM AN ADVOCATE POINT OF VIEW WHERE WE'RE TRYING TO MOVE AS QUICKLY AS POSSIBLE, THE MORE DYNAMIC WE CAN BE IN INFORMATION SHARING, THE BETTER PRODUCT WE'LL HAVE AND THE FASTER WE'LL GET SOMETHING.

CHAIRMAN LO: SO THAT'S VERY HELPFUL, THAT CLARIFICATION. IT'S REALLY BEING INVOLVED IN THE GRANTS REVIEW PROCESS WITH A VIEW OF HELPING TO

STRENGTHEN THE GRANTS THAT ARE FUNDED.

MR. SHEEHY: POTENTIALLY FOR SCNT UNLESS THERE'S A SENSE THAT THERE'S A LOT OF THE COMFORT LEVEL ON DONOR PROGRAMS WITHIN THIS GROUP THAT --

CHAIRMAN LO: LET ME SAY TO MAKE SURE I'VE SUMMED IT UP. I'VE HEARD PAT, I THINK, SAY SOMETHING A LITTLE DIFFERENT WITH WHY IT'D BE USEFUL FOR US TO REVIEW PROTOCOLS, WHICH IS REALLY TO HELP US SORT OF CLARIFY OUR OWN THINKING ABOUT WHAT SOME OF THE PROBLEMS ARE SORT OF ON THE GROUND IN REAL LIFE, WHICH MAY SIGNAL MAYBE MORE SORT OF A LONGER TERM BENEFIT, THAT IT HELPS US KEEP AHEAD OF THE SITUATION. AND EVEN THOUGH IT MAY NOT FEED BACK TO THAT SPECIFIC PROJECT OR CYCLE, IT WILL HELP IN THE LONG RUN.

MS. KING: IT'S NOT ANTAGONISTIC TO WHAT JEFF JUST SAID. IT MEANS THAT SUCH A PROCESS COULD HAVE SEVERAL OBJECTIVES, ALL OF WHICH WE MIGHT THINK WOULD STRENGTHEN THE OVERALL PROGRAM AND WHAT WE'RE TRYING TO DO.

CHAIRMAN LO: NOW, I DON'T KNOW -- SO LET ME JUST TRY AND DEAL WITH EACH OF THESE BECAUSE THEY ARE, I THINK, AT DIFFERENT LEVELS OF DEVELOPMENT. FOR THE BEST PRACTICE GUIDELINES, THIS IS SOMETHING THAT I TALKED A LOT TO ZACH HALL ABOUT BEFORE HE LEFT, TRYING TO THINK OF HOW TO DO THAT. AND, AGAIN, WE WERE

THINKING VERY MODESTLY, I THINK, OF TRYING TO JUST BRING TOGETHER THE BEST CLINICAL EXPERIENCE AND WISDOM AND SORT OF MAKE IT MORE COHERENT AND CONSISTENT. AND CONVENING A RELATIVELY SMALL GROUP OF ART EXPERTS, I WOULD ADD OF THE VERY IMPORTANT SUGGESTION PAT MADE, THAT WE INCLUDE PEOPLE WITH A LOT OF EXPERIENCE DEALING WITH DONORS WHO WEREN'T WELL-TO-DO WHITE WOMEN. AND WE THOUGHT THAT THOSE SHOULD BE FROM OUT OF STATE.

WE ACTUALLY HAVE GONE A STEP FURTHER AND LOOKED AROUND AND SAID WHO COULD BE ON THE COMMITTEE, AND ONE NAME THAT CAME UP WAS RALPH CHANDLER, WHO IS ON THIS COMMITTEE, BUT BEING NOW FROM ATLANTA IS NOT ELIGIBLE TO APPLY FOR CIRM GRANTS. SO IT KIND OF RELIEVES ANY CONCERNS THAT SOMEHOW SOMEONE IN CALIFORNIA GETS ON THE COMMITTEE AND THEN THEIR GROUP IS THE ONE THAT CIRM IS GOING TO FEED ALL THE DERIVATIONS TO AND HAVE STARTED TO THINK OF WHAT OTHER PEOPLE MIGHT WANT TO SERVE ON THE COMMITTEE. AND WE WERE TRYING TO THINK OF PEOPLE WHO ARE EXPERIENCED IN THE ART WHO HAD BOTH CLINICAL AND SORT OF POLICY EXPERIENCE, SO PEOPLE WHO HAVE HELD LEADERSHIP POSITIONS IN THEIR OWN CLINICAL ORGANIZATION OR PERHAPS PROFESSIONAL SOCIETIES, AND CLEARLY WANTING TO HAVE A REPRESENTATIVE COMMITTEE. SO HAVING A WOMAN AS CO-CHAIR, I THINK HAVING PEOPLE WHO ARE EITHER

THEMSELVES FROM PERSONS OF COLOR OR HAVE A LOT OF PATIENTS WHO ARE OOCYTE DONORS IN THAT GROUP WOULD REALLY MAKE SURE WE'RE NOT JUST SORT OF TALKING ABOUT CERTAIN PEOPLE.

SO THAT I THINK WE'VE THOUGHT SOME ABOUT IT, AND WE'RE NOW SORT OF TRYING TO THINK OF HOW TO ACTUALLY DO IT WITHIN CIRM. I TAKE IT BECAUSE OF THE BUDGET LIMITATIONS AND THINGS, THERE ARE QUESTIONS OF HOW TO ACTUALLY CONSTITUTE THAT. SO I THINK I'D LIKE TO SORT OF GET SOME FEEDBACK.

THE OTHER TWO IDEAS, I THINK, ARE NEW AND WE NEED TO THINK MORE ABOUT. THE SECOND BIG ISSUE WOULD BE THE ONE YOU RAISED, JEFF. HOW CAN WE AS A WORKING GROUP CONTRIBUTE TO CIRM AS A WHOLE AS THESE NEW PROTOCOLS COME IN THAT DEAL WITH OOCYTE DONATION FOR SCNT LINES? WHAT ROLE COULD WE PLAY THAT'S CONSTRUCTIVE BOTH TO THE GRANTEES OR THE APPLICANTS TO THE REVIEW PROCESS TO CIRM AS A WHOLE WITH THE ADDED EXTRA THAT WE WOULD SORT OF JUST BECOME MORE KNOWLEDGEABLE IN THAT SENSE? I'M A LOT LESS SURE OF HOW TO DO THAT BECAUSE I MUST CONFESS I DON'T KNOW AS MUCH ABOUT THE GRANTS REVIEW PROCESS AND HOW IT WORKS AND HOW WE MIGHT FIT IN WITH THAT.

I THINK THE THIRD THING, WHICH GOES BACK TO KEN OLDEN'S IDEA, TRYING TO MOVE TOWARDS GETTING MORE

EMPIRICAL DATA, I'M EVEN LESS CLEAR ABOUT HOW TO DO THAT. I THINK JUST TO SAY CIRM YOU OUGHT TO DO THIS, IF WE CAN TRY AND FLESH THAT OUT A BIT, BUT IT STRIKES ME THAT WE'RE AT DIFFERENT STAGES OF THAT. WE MAY ACTUALLY COME BACK TO THIS. WE'RE GOING TO HAVE A BRIEF REPORT ON THE GRANTS PROCESS TOMORROW; IS THAT RIGHT?

DR. LOMAX: WELL, THE REPORT TOMORROW IS INTENDED TO BE SORT OF A SUMMARY OF HOW THE GRANTS ADMINISTRATION IS EVOLVING. AND THAT'S, AGAIN, SORT OF A CONTINUATION. WE HEARD ABOUT GRANTS ADMINISTRATION POLICY, SO THAT'S SORT OF A TRADITIONAL ITEM THAT'S BEEN BROUGHT TO THIS GROUP. I DON'T THINK WE'RE GOING TO BE -- THIS TYPE OF ISSUE WASN'T ENVISIONED.

CHAIRMAN LO: WASN'T ENVISIONED. OKAY.

DR. TAYLOR: BERNIE, YOU'VE LAID THAT OUT NICELY AS SORT OF THREE SORT OF OBJECTIVES. I ACTUALLY THINK THAT THE FIRST TWO MIGHT BE MERGED IN A WAY IN THAT IF YOU COULD PUT TOGETHER THE SECOND PART, SO YOUR EXERT PANEL, WHICH I THINK IS ACTUALLY MATURING AS WE KIND OF DISCUSSED IT, SO THAT THERE WOULD BE BOTH REPRESENTATION OF POPULATIONS THAT MAY BE RELATIVELY UNDER REPRESENTED. AND THE DATA THAT EXISTS CURRENTLY, THERE'S ALSO, I THINK, AN IMPORTANT COMPONENT OF USING PEOPLE FROM MANDATED STATES WHERE IVF PRACTICES ARE

MANDATED AND COVERED BY AN INSURANCE COMPANY WHICH SORT OF GIVES A BROADER REPRESENTATION, AND MASSACHUSETTS IS AN EXCELLENT EXAMPLE WHERE YOU HAVE KIND OF A MORE DIVERSE POPULATION. THAT WOULD, I THINK, BE EXTREMELY IMPORTANT.

BUT IF A CERTAIN NUMBER OF REPRESENTATIVE PROTOCOLS THAT CAME FROM APPLICANTS COULD BE REVIEWED BY A SUBCOMMITTEE AND FED INTO THAT EXPERT PANEL, BECAUSE A LOT OF THESE PEOPLE, FRANKLY, I THINK THE CLINICAL EXPERTS IN THIS AREA WOULDN'T HAVE THOUGHT A LOT ABOUT THE ETHICAL AND SORT OF PRACTICAL ISSUES OF OOCYTE DONATION FOR SCNT. I THINK IF YOU COULD FUNNEL SOME OF THOSE PROTOCOLS TO THAT PANEL, IT WOULD BE A PRETTY GOOD SUBSTRATE FOR THEM TO SORT OF CHEW ON AND TO THINK A LITTLE BIT ABOUT HOW THEY WOULD WANT TO CONSTRUCT THE TYPES OF RECOMMENDATIONS OR GUIDELINES THAT THEY MIGHT COME UP WITH. SO I THINK THOSE TWO COULD ALMOST BE OVERLAPPING.

THE THIRD PART, WHICH IS REALLY GETTING GOOD DATA, THAT I THINK IS A MUCH BIGGER AND, FRANKLY, MORE CHALLENGING ISSUE, AND I DON'T HAVE A BRILLIANT SOLUTION FOR THAT ONE.

CHAIRMAN LO: ANN, HI. WELCOME. GLAD TO HAVE YOU.

DR. KIESSLING: SORRY I'M LATE. ACTUALLY I'M

REALLY SORRY I'M LATE. WOULD IT BE -- WHAT I UNDERSTAND THAT YOU'RE TRYING TO DO, AND I'M SORRY I'M SO LATE, BUT WE'VE SORT OF SKIRTED AROUND THIS ISSUE FOR QUITE A WHILE NOW ABOUT WHETHER WE WERE GOING TO ACTUALLY DESIGN BEST PRACTICE, AND IT'S SORT OF COME AND GONE. NOW IT SEEMS LIKE JEFF IS HOPING THAT WE'D DO THAT, RIGHT? IS THAT WHERE YOU ARE? YOU'RE SORT OF HOPING THAT EVEN IF IT'S HALF A DOZEN STEPS.

MR. SHEEHY: IT DIDN'T COME NECESSARILY FROM ME, BUT HAVING -- WELL, YOU KNOW, HAVING SEEN AN SCNT GRANT THAT REALLY TROUBLED ME AND NOT SEEING ANY REAL MECHANISM TO GET A GRIP ON IT OTHER THAN RELYING ON A PRIVATE IRB TO POLICE IT, AND LUCKILY FOR ME THE *L.A. TIMES* HAS SUBMITTED THE GRANT TO A GREATER DEGREE OF SCRUTINY. BUT THERE'S NOT A MECHANISM. JUST FEELING LIKE THESE THINGS, KIND OF THEY'RE OUT AND THEN THEY'RE GONE.

DR. KIESSLING: WOULD IT BE VALUABLE TO GET SOME INPUT ACTUALLY FROM OTHER COUNTRIES? IF YOU'RE INTERESTED IN A BROADER RANGE OF, FOR INSTANCE, ETHNIC RESPONSE, OTHER COUNTRIES PRACTICE. AND SOME COUNTRIES HAVE VERY RESTRICTED GUIDELINES FOR WHAT THEY CAN DO. DENMARK, YOU HAVE TO MAINTAIN A VERY HIGH PREGNANCY RATE WITH A VERY TINY AMOUNT OF HORMONE. I JUST WONDER IF THAT WOULD BE OF SOME VALUE RATHER THAN JUST LOOKING

AT -- AND IF YOU HAD SOME SOUTH AMERICAN PROGRAMS LIKE THE PROGRAMS IN CHILE WHERE THEY ARE VERY RESTRICTED IN TERMS OF WHAT THEY CAN DO BECAUSE THEY HAVE TO TRANSFER BACK EVERYTHING THEY FERTILIZE. I DON'T KNOW THAT YOU WANT THIS TO BE A HUGE PANEL, BUT IT MIGHT BE GOOD TO GET THE INPUT OF FOLKS WHO ARE DEALING WITH ANOTHER STRAIN OF PEOPLE.

CHAIRMAN LO: THAT'S ACTUALLY A GOOD SUGGESTION.

DR. OLDEN: WE RAISED THAT EARLIER WHEN THE PRESENTATION WAS RAISED, AND WE THOUGHT DENMARK SHOULD BE A PLACE WITH GOOD DATA. YOU'RE RIGHT. SOME FROM SOUTH AMERICA AS WELL.

DR. TAYLOR: BUT I THINK WE'RE REALLY INTERESTED IN DONOR CYCLES, AND THAT IS MORE DIFFICULT TO SORT OF PUT YOUR FINGER ON. SO THE SWITZERLAND AND DENMARK HAVE VERY RESTRICTIVE PROGRAMS FOR THEIR IVF, BUT HOW MUCH IS REALLY KNOWN ABOUT DONOR PROGRAMS WITHIN THOSE COUNTRIES? THAT WAS ONE OF THE QUESTIONS THAT WE RAISED TO DR. GUIDICE. I THINK IT'S NOT SO RELEVANT. IT'S PROBABLY MORE RELEVANT TO THE DONOR POPULATION, FRANKLY, WHEN YOU'VE GOT VERY RESTRICTIVE IVF REGULATIONS, BUT IT STILL DOESN'T SEEM TO BE AS REPRESENTATIVE OF THOSE WOMEN WHO ARE NOT GOING TO BE AT RISK OF PREGNANCY.

DR. KIESSLING: DID YOU TOUCH ON THE CONCEPT OF EGG SHARING? DID I MISS THAT?

DR. TAYLOR: SHE RAISED THAT.

CHAIRMAN LO: ANN, SO THAT WE TRY AND FILL YOU IN. SO WHAT WE'RE TALKING ABOUT IS SORT OF GUIDELINES REALLY FOR THE MEDICAL QUESTION OF HOW CAN YOU MINIMIZE THE RISK OF MEDICAL COMPLICATIONS. SO AS YOU KNOW, WE'VE TALKED A LOT ABOUT PSYCHOLOGICAL SCREENING AND SORT OF ASSESSING COMPREHENSION AND LACK OF DURESS AND THINGS. AND THIS REALLY WAS MEANT TO COME OUT OF THIS WORKSHOP AND SORT OF TO PROVIDE A LITTLE MORE GUIDANCE TO INVESTIGATORS AND SCRO'S OR IRB'S AS TO SORT OF WHAT EXACTLY DO WE MEAN BY SCREENING OR MONITORING?

CERTAINLY I THINK WE COULD GET -- I THINK YOUR IDEA OF GOING TO OTHER PARTS OF THE WORLD WHO HAVE A LOT MORE EXPERIENCE WITH WOMEN WHO AREN'T CAUCASIAN, AREN'T NECESSARILY UPPER CLASS, BECAUSE IT MAY BE COVERED BY INSURANCE, WOULD CERTAINLY GIVE US A WINDOW ON IF THEY SAY, WELL, WE TRIED WHAT THEY DID IN NEW YORK AND IT DOESN'T WORK FOR US BECAUSE DA-DA-DA-DA, THE DOSES HAVE TO BE DIFFERENT, THAT WOULD BE EXTREMELY HELPFUL. I THINK WE CERTAINLY SHOULD BE ABLE TO GET THAT INFORMATION AS INPUT TO THE COMMITTEE. WHETHER OR NOT WE CAN GET ONE OF THE PANELISTS OR THE CONSULTANTS

TO BE FROM OTHER AREAS, I THINK, GETS INTO QUESTIONS OF FEASIBILITY AND BUDGET, BUT I THINK WE SHOULD BE ABLE TO GET THE INFORMATION OF DOES THIS SEEM -- WOULD THAT WORK IN YOUR POPULATION? IF NOT, HOW DO YOU DO IT? WHAT'S THE REASONING? WHAT'S YOUR EXPERIENCE?

DR. ROWLEY: I THINK WE SHOULD BE REALLY CAREFUL. AND I COME BACK AND QUESTION BOB AND HIS IDEA OF COMBINING THINGS. IF, IN FACT, ONE GOAL IS TO TRY TO GET SOME KIND OF GUIDELINES THAT SEEM REASONABLE IN THE INTERIM, THEY'RE GOING TO HAVE THEIR LIMITATIONS AND THEIR DEFECTS, BUT SHOULD WE PUSH FOR THAT AND, THEREFORE, IT WOULD BE A SMALLER COMMITTEE, REALIZING THAT THIS OTHER INFORMATION CAME FORWARD, YOU MODIFY THE GUIDELINES. AND SO I GUESS IT'S A MATTER OF PRIORITIES. IF GOOD PRACTICES GUIDELINES, REALIZING THAT THEY ARE FLAWED AND, THEREFORE, TEMPORARY, IF YOU WILL, OR SOME ASPECTS MIGHT BE TEMPORARY, SHOULD WE AS A GROUP SUPPORT A MORE LIMITED FIRST STEP WITH THE NOTION THAT WE ARE SUPPORTING THE OTHER ASPECTS, BUT THEY MAY TAKE MORE TIME TO IMPLEMENT IN A THOUGHTFUL WAY?

CHAIRMAN LO: WE HAVE TENDED TO TAKE A POSITION HERE ON THIS COMMITTEE THAT WE ARE ALWAYS OPEN TO MODIFYING OUR THINKING BASED ON MORE DATA, OTHER EXAMPLES. SO I LIKE THE IDEA OF INTERIM GUIDANCE

SUBJECT TO CHANGE.

WE'VE HAD A LOT OF DISCUSSION, WHICH I THINK HAS BEEN USEFUL. I WANT TO MAKE SURE WE GET SOME PUBLIC INPUT. I DON'T KNOW IF THERE ARE PEOPLE IN THE PUBLIC WHO WANT TO COMMENT ON THE DISCUSSION WE'VE HAD AFTER THE BREAK. IF SO, MAYBE THIS WILL BE A GOOD TIME TO GIVE YOU ALL A CHANCE TO MAKE YOUR COMMENTS.

JUST FOR THE RECORD, INTRODUCE YOURSELF AND WHO YOU ARE BEFORE YOU SPEAK.

MS. CROWLEY: I'M SHANNON SMITH CROWLEY, REPRESENTING THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE. I HAD CHECKED IN EARLIER WITH THE ASRM TO SEE IF THEY HAD SPECIFIC PRACTICE GUIDELINES ABOUT THIS PROCESS, AND THEY HAD NOT YET DEVELOPED SOMETHING THEMSELVES. AND SO LOOKING AT THIS ISSUE THAT YOU'RE TALKING ABOUT IN TERMS OF HAVING SUFFICIENT EVIDENCE TO GO FORWARD IS VERY PROBLEMATIC. IT LOOKS LIKE YOU DO HAVE A NUMBER OF THINGS THAT ARE SUGGESTED WHERE YOU, FOR INSTANCE, EXCLUDE WOMEN THAT HAVE CERTAIN CONDITIONS, AND THERE'S A LOT OF THINGS THAT YOU CAN DO TO BE VERY SAFE AND MAYBE GO FURTHER THAN YOU WOULD IN AN IVF SITUATION.

BUT FOR A DONOR SITUATION, FOR INSTANCE, A CERTAIN BODY MASS INDEX, THE POLYCYSTIC OVARIAN SYNDROME, THOSE SORTS OF THINGS WHERE THERE'S NOT

REALLY QUITE THE SAME BENEFIT THERE, THAT YOU CAN CERTAINLY EXCLUDE THOSE.

ONE OF THE PROBLEMS WE HAVE WITH GETTING A LOT OF SPECIFICITY INTO THE GUIDELINES IS, AND I THINK ALL OF YOU WERE SAYING THIS, IS THAT THIS IS A FIELD THAT EVOLVES QUICKLY AND MAY BE OUT OF DATE, AND YOU DON'T NECESSARILY WANT TO HAVE PEOPLE BE HELD TO CERTAIN GUIDELINES THAT MAY END UP BEING WORSE THAN WHAT YOU WANT. SO JUST I WOULD ENCOURAGE YOU TO HAVE MAYBE SOME BROAD PARAMETERS AND ALLOW FOR SOME CONTINUED FLEXIBILITY.

DR. PETERS: MAY I ASK SHANNON A QUESTION? SHANNON, WHAT DO YOU THINK ABOUT KEN OLDEN'S POINT EARLIER, THAT THE DEGREE OF RISK FOR AN EGG DONOR FOR RESEARCH OUGHT TO BE MUCH SMALLER THAN THAT FOR SOMEONE WHO IS PLANNING A PREGNANCY? DO YOU THINK JUST THE SHEAR EXCLUSION, THEN, OF MORE WOMEN FROM DONATING EGGS FOR RESEARCH WOULD ACCOMPLISH WHAT KEN IS ASKING FOR? AND DO YOU THINK THAT WE CAN EASILY COME UP WITH THE CRITERIA FOR THAT EXCLUSION?

MS. CROWLEY: I THINK YOU COULD BEGIN A LIST FOR EXCLUSIONS. AND THAT, AGAIN, LOOKING AT THE RISK BENEFIT, AND THIS BEING A DONOR POPULATION VERSUS IVF, THAT IT WOULD MAKE MORE SENSE THAN TO SAY TO SOMEBODY WHO HAS POLYCYSTIC OVARIAN SYNDROME WHO WANTS TO HAVE A

BABY, SAYING YOU CAN'T PARTICIPATE IN IVF, THAT'S NOT REALISTIC OR FAIR TO THAT WOMAN. BUT THERE MAY NOT BE THE NEED FOR THAT WOMAN IF WE'VE GOT OTHER WOMEN IN THE POPULATION TO DONATE.

ONE OF THE THINGS, WHEN I WENT TO THE IOM MEETING IN SEPTEMBER, AND I THOUGHT IT WAS A FABULOUS MEETING, SOME OF THE THINGS THAT THEY REALLY BROUGHT OUT WERE, AND I THINK DR. GUIDICE DID AN EXCELLENT JOB, BUT I WANTED TO REITERATE WAS THE RISK FOR THE HYPERSTIMULATION SYNDROME IS GOING TO BE MANY FOLDS TIME HIGHER FOR A WOMAN WHO IS DOING THIS PROCESS FOR IN VITRO FERTILIZATION BECAUSE SHE WILL BE PREGNANT AND HER HORMONES WILL BE DIFFERENT. ESSENTIALLY ONCE SHE'S COMPLETED THE PROCESS FOR DONATION AND THE HORMONES DROP OFF, THE LATE HYPERSTIMULATION SYNDROME VIRTUALLY GOES AWAY. SO JUST THE FACT THAT YOU'RE DEALING WITH A DONOR POPULATION VERSUS FOR FERTILITY, YOU ARE GOING TO HAVE A MUCH LOWER RISK OF THAT SYNDROME IN THE FIRST PLACE. AND THEN THERE ARE KNOWN CONDITIONS THAT ARE GOING TO MAKE THIS RISKIER, AND YOU CAN START TO EXCLUDE THOSE.

DR. PETERS: THANKS A LOT.

CHAIRMAN LO: SHANNON, BEFORE YOU SIT DOWN, COULD I ASK YOU A CLARIFICATION? AND YOU MAY NOT KNOW THIS, BUT IF YOU COULD FIND OUT, THAT WOULD BE GREAT.

LINDA GUIDICE GAVE US A COPY OF -- THESE ARE THE ASRM GUIDELINES IN *FERTILITY AND STERILITY* ON OVARIAN HYPERSTIMULATION SYNDROME. SO YOU'RE SAYING SART DOES NOT HAVE ITS OWN SET OF GUIDELINES OR PRACTICE PARAMETERS, WHATEVER YOU WANT TO CALL THEM, ON OHSS?

MS. CROWLEY: THANK YOU FOR ASKING FOR THE CLARIFICATION. MY COMMENT WAS MORE TO PROTOCOLS FOR THE ENTIRE PROCESS OF THE STIMULATION RATHER THAN SPECIFICALLY IN MANAGING THE HYPERSTIMULATION SYNDROME.

DR. ROWLEY: CAN I ASK BECAUSE ALSO IN THIS GUIDELINE RISK FACTORS INCLUDE LOW BODY WEIGHT. AND WHAT WE WERE TOLD IN THE PRESENTATION WAS THAT IT'S INCREASED BODY MASS, BMI, THAT'S A RISK FACTOR. AND THEY WOULD SEEM TO BE EXACTLY OPPOSITE.

MS. CROWLEY: I CAN'T ANSWER THAT SPECIFIC QUESTION. I'D HAVE TO ASK DR. GUIDICE FOR THAT.

CHAIRMAN LO: JUST A POINT OF INFORMATION.

DR. ROWLEY: WHAT DO YOU THINK, ROBERT?

DR. TAYLOR: RISKS ARE PROBABLY HIGH AT BOTH EXTREMES OF THE WEIGHT RANGE MOSTLY BECAUSE OF THE KIND OF DOSAGE-TO-VOLUME DISTRIBUTION AND THE STIMULATION OF THE OVARIES IN A SMALL WOMAN.

CHAIRMAN LO: CAN I ASK ONE MORE THING, SHANNON, JUST TO CLARIFY? CAN YOU JUST EXPLAIN TO US BRIEFLY THE DISTINCTION BETWEEN SART AND ASRM?

MS. CROWLEY: ASRM IS A SOCIETY OF APPROXIMATELY 9,000 PROFESSIONALS, PHYSICIANS, NURSES, SCIENTISTS, THAT ARE IN THE REPRODUCTIVE HEALTH FIELD. SART IS A SISTER ORGANIZATION, AND IT'S MORE FOR THE ACTUAL FACILITIES THAT ARE PERFORMING THE IN VITRO FERTILIZATION.

CHAIRMAN LO: SO I'M THINKING VIN DIAGRAMS, THERE'S SOME OVERLAP, BUT THERE'S ALSO A LOT OF DIFFERENCE?

MS. CROWLEY: CORRECT.

DR. TAYLOR: SART USUALLY DOESN'T PROMULGATE A LOT OF GUIDELINES. THEY TEND TO BE MORE ON THE SORT OF DATA RECEPTION SIDE OF THINGS, AND THEY DO --

CHAIRMAN LO: AS IN SORT OF THE OUTCOMES.

DR. TAYLOR: -- MONITOR THE CLINICS AND THAT SORT OF THING.

MS. CROWLEY: IF YOU WOULD LIKE, I CAN GIVE TO THE GROUP, I BROUGHT WITH ME A LIST OF ALL OF THE DIFFERENT ISSUE AREAS WHERE ASRM HAS TAKEN POSITION PAPERS OR COMMENT AREAS SO YOU CAN SEE THE KIND OF THINGS WHERE THEY DO HAVE DIFFERENT GUIDELINES AND DIFFERENT RECOMMENDATIONS IF YOU WOULD LIKE THAT.

CHAIRMAN LO: INFORMATION IS ALWAYS HELPFUL. THANKS. OTHER MEMBERS OF THE PUBLIC WANT TO COMMENT? OKAY. SO I'M TRYING TO SORT OF THINK OF WHERE WE ARE.

LET ME TAKE A STAB JUST TO SORT OF SEE IF WE CAN GET US ROLLING.

AGAIN, I'LL TRY AND BREAK INTO THREE AREAS, BUT WE'VE SORT OF SAID HOW WE NEED THEM TO OVERLAP AND REINFORCE EACH OTHER, AND THEY MAY HAVE DIFFERENT TIMELINES. ONE WOULD BE TO CONVENE A GROUP OF CONSULTANTS TO DEVELOP INTERIM BEST PRACTICE GUIDELINES ON MINIMIZING THE RISK OF OHSS IN OOCYTE DONORS. AND WE WOULD WANT THAT TO BE ON A RELATIVELY SHORT TIMELINE BECAUSE WE'D LIKE IT TO BE IN PLACE AS INVESTIGATORS BEGIN TO DEVISE PROTOCOLS AND DIFFERENT ORGANIZATIONS TO REVIEW THOSE PROTOCOLS.

WE WOULD WANT THAT COMMITTEE TO HAVE EXPERTISE AND EXPERIENCE WITH CARRYING OUT OOCYTE RETRIEVAL IN A VARIETY OF POPULATIONS, AND WE MENTIONED A NUMBER OF STRATEGIES FOR DOING THAT. GOING TO STATES, GETTING SOME MEMBERS FROM STATES THAT HAVE HEALTH COVERAGE, INSURANCE COVERAGE, WHICH TENDS TO BROADEN THINGS OUT A LITTLE BIT, GOING TO OTHER COUNTRIES THAT HAVE POPULATIONS WHICH ARE DIFFERENT THAN THE PREDOMINANT POPULATION THAT RECEIVES IVF IN THIS COUNTRY. AND THAT WE ALSO WOULD WANT, IF POSSIBLE, AND I CAN THINK OF SOME WAYS TO DO THAT, GEOFF. I MAY BE ABLE TO MAKE AVAILABLE -- HAVE SOME OF OUR INVESTIGATORS MAKE AVAILABLE THEIR PROTOCOLS TO

THIS COMMITTEE ON THE GROUNDS THAT HAVING ACTUAL PROTOCOLS TO LOOK AT WOULD HELP THIS GROUP OF CONSULTANTS TO INFORM THEIR DELIBERATIONS. SO THAT'S ONE.

I ALMOST WANT TO SORT OF ASK IF WE WOULD BE WILLING TO SORT OF CHARGE, I GUESS IT WOULD BE, GEOFF WITH KIND OF TRYING TO FIGURE OUT HOW TO SET THIS UP. THE NOTION WOULD BE THIS GROUP OF EXPERT CONSULTANTS WOULD REPORT BACK TO THIS GROUP, WHICH WOULD THEN DISCUSS, DELIBERATE, REFINE WITH PUBLIC COMMENT, AND WE WOULD SORT OF PRESENT THAT TO ICOC, GEOFF. SO IT WOULD BE SEVERAL DIFFERENT STEPS.

ANOTHER THING IS I GUESS FOR US TO THINK MORE ABOUT HOW THIS GROUP COULD BE INVOLVED NOT JUST IN THAT FIRST ACTIVITY, BUT IN THE EXAMINATION OF PROTOCOLS BEING DEVELOPED AND SUBMITTED, WHETHER IT'S PART OF A REVIEW PROCESS, BUT WE DON'T WANT TO INTERFERE WITH THE GRANTS WORKING GROUP, WHETHER WE CAN BE OF USE TO THEM, WHETHER WE CAN BE OF USE TO IRB'S OR SCRO'S. I THINK THERE'S SOME SENSE THAT MAYBE WE HAVE A ROLE TO PLAY IN KIND OF HELPING TO THINK THROUGH THE ISSUES THAT ARE COMING UP WITH CERTAIN TYPES OF RESEARCH. I THINK OOCYTE DONATION, AS WE'VE SAID, FOR RESEARCH TENDS TO BE ONE OF THESE SENSITIVE AREAS WHERE WE REALLY WANT TO GIVE IT GOOD THOUGHT. I'M NOT QUITE AS CLEAR HOW WE

CAN DO THAT INSTITUTIONALLY, BUT I HAD A SENSE THAT SEVERAL PEOPLE THOUGHT THIS WOULD BE AN IMPORTANT THING, A VALUABLE THING FOR US TO DO, AND I THINK WE NEED TO -- I'D LIKE TO GET A SENSE OF DO WE ALL THINK THAT, AND THEN WE WOULD NEED TO THINK MORE HOW TO DO IT.

AND THE FINAL THING, AGAIN, WE WANT TO INTERFACE WITH THE OTHER TWO IS TO TRY AND ENCOURAGE COLLECTION OF MORE AND BETTER EMPIRICAL DATA ON RISK TO OOCYTE DONORS, AND PART OF THE BETTER IS JUST BETTER DATA IN TERMS OF TAKING MORE PRECISE DEFINITIONS AND STANDARD DEFINITIONS AND MAKING SURE WE TAKE INTO ACCOUNT THE WOMAN WITH OHSS, DID SHE GET PREGNANT OR NOT, BUT ALSO BEING MORE INCLUSIVE IN TRYING TO COLLECT DATA ON GROUPS THAT ARE DIFFERENT THAN THE POPULATIONS WHO ARE PROVIDING THE DATABASE WITH CURRENT DATA. AND I THINK PART OF IT MAY BE TRYING TO SORT OF PUSH AHEAD PART OF THE STRATEGIC PLAN. AGAIN, I'M NOT QUITE CLEAR HOW WE WANT TO DO THAT AND HOW FAR THIS IS OUR CHARGE AS OPPOSED TO OUR GIVING A STRONG RECOMMENDATION TO EITHER THE ICOC OR TO THE NEW PRESIDENT OF CIRM OR TO THE GRANTS WORKING GROUP OR THE STRATEGY WORKING GROUP. I'M NOT QUITE SURE HOW MUCH WE NEED TO DO, BUT WE OBVIOUSLY HAVE PEOPLE WHO HAVE THOUGHT A LOT ABOUT IT.

THAT'S HOW I'M SORT OF THINKING THROUGH

THINGS AT THIS POINT. I JUST WANT TO SORT OF, ASSUMING THAT WASN'T OUR DINNER THAT CRASHED TO THE FLOOR, I WANTED TO TRY AND SORT OF MOVE US ALONG HERE.

DR. KIESSLING: BERNIE, ARE YOU THINKING OF SORT OF LIKE A DONOR REGISTRY?

CHAIRMAN LO: I'M NOT --

DR. KIESSLING: JEFF, IS IT YOUR SENSE THAT THERE WOULD BE FUNDS AVAILABLE TO ORGANIZE LIKE AN EGG DONOR REGISTRY? THAT WOULD JUST BE AWESOME.

MR. SHEEHY: I THINK THERE'S -- AS GEOFF LOMAX NOTED, WITHIN THE STRATEGIC PLAN THERE IS FUNDING ALLOCATED TO COLLECT -- TO DO THIS SORT OF DATA COLLECTION. I THINK WE COULD PUT AN RFA TOGETHER FOR WHATEVER PARTICULAR PROCESS.

DR. KIESSLING: WE'VE ACTUALLY TALKED ABOUT THAT BEFORE.

MR. SHEEHY: IN A WAY THIS IS WHERE THE THINKING NEEDS TO COME FROM, AND IT'S NOT EVER GOING TO BE SLOW. AND THERE REALLY IS NOT A FUNDING SHORTAGE AT THIS TIME. RIGHT. AND PRESUMABLY BY THE END OF THE SUMMER, WE SHALL HAVE SOME FINAL DISPOSITION OF THE LAWSUIT, HOPEFULLY FAVORABLY, AND THEN THERE REALLY WON'T BE A FUNDING SHORTAGE. SO IT JUST SEEMS TO ME THAT THIS ONE ISSUE ON OOCYTE DONATION IS ONE THAT'S IMMEDIATE, AND IT'S NOT GOING TO DO US ANY GOOD TO FUND

A STUDY THREE YEARS DOWN THE ROAD TO SEE WHAT'S BEEN GOING ON FOR THE PAST UMPTEEN YEARS. WHEN THE STUDY IS FINISHED, WE'LL HAVE A NICE RETROSPECTIVE.

I REALLY THINK THAT WHAT I'M HEARING IS THAT WE NEED DATA NOW, AND WE SHOULD DIRECT THE -- WE SHOULD SEND IN THE REPORT THAT GOES UP TO THE ICOC A STRONG SIGNAL THAT THE DATA NEEDS TO BE COLLECTED. I THINK THAT THIS HAS BEEN A NON -- THIS WAS CONSIDERED TO BE THE MOST CONTROVERSIAL SET OF ISSUES THAT WE WOULD FACE AS AN ENTITY. AND BECAUSE OF THE EXTRAORDINARY WORK OF THIS COMMITTEE, IT HAS NOT BEEN, AND I THINK THAT THE ICOC WOULD RESPECT THE DILIGENCE AND THE DELIBERATE WAY IN WHICH THIS COMMITTEE HAS CONDUCTED ITSELF, THAT THEIR RECOMMENDATIONS WOULD HAVE STRONG WEIGHT. I THINK THAT WE HAVE THE ABILITY TO DO THIS. IT'S JUST WHAT SHOULD WE DO, AND THAT'S WHY THIS COMMITTEE EXISTS.

DR. TAYLOR: WELL, IF THERE ARE ABOUT 15,000 DONOR CYCLES IN THE COUNTRY, I WOULD GUESS THAT ABOUT 20 PERCENT OF THOSE ARE HAPPENING IN CALIFORNIA. THAT WOULD BE A PRETTY GOOD -- ANNUALLY. THAT'S A PRETTY GOOD NUMBER TO FLOAT AN RFA TO TRY TO COLLECT SOME OF THAT DATA AND TO --

DR. KIESSLING: SOME OF IT'S GOING TO BE IN THE SART DATABASE, RIGHT?

DR. TAYLOR: THERE'S NOT A LOT ON DONORS. THERE'S A LOT ON DONOR -- THE RECIPIENTS. WE'VE GOT THOSE DATA PRETTY WELL COVERED. WHAT I'M THINKING OF IS IF WE LOOK NATIONALLY, WE'D BE ABLE TO COLLECT AND PROBABLY MORE -- WELL, MORE INTERESTING. IT WOULD BE INTERESTING TO GET THAT DATA, BUT I THINK IT WOULD BE AWFULLY HARD TO JUSTIFY, THINKING OFF TOP OF MY HEAD, CIRM FUNDING A NATIONAL STUDY. IF YOU JUST LOOKED AT THE PROGRAMS ACROSS CALIFORNIA AND HAD A CALIFORNIA RFA FOR CIRM FUNDING FOR THIS, I WOULD THINK THAT IN A COUPLE OF YEARS YOU COULD HAVE SOME PRETTY INTERESTING INFORMATION.

CHAIRMAN LO: WELL, THERE ARE TWO ISSUES I THINK WE HAVE TO THINK THROUGH WITH REGARD TO A DATABASE. ONE, I THINK ARE WE GOING TO HAVE A DATABASE OF OOCYTE DONORS FOR RESEARCH OR ALL OOCYTE DONORS?

DR. TAYLOR: WELL --

DR. KIESSLING: I WOULD THINK YOU WOULD DO IT FOR RESEARCH. I REALLY AGREE WITH KEN. I REALLY THINK THAT THE RISK TO THESE DONORS FOR RESEARCH NEEDS TO BE ZERO. AND I DON'T THINK THAT THE RISK -- I THINK THE INFERTILITY CLINICS -- I DON'T THINK WE WANT TO BE IN THE BUSINESS OF REGULATING INFERTILITY CLINICS, BUT I THINK THAT WE DO WANT TO BE IN THE BUSINESS OF OVERSEEING AND PROTECTING HUMAN SUBJECTS RESEARCH. I

THINK THAT'S A BIG DIFFERENCE, AND I THINK THAT YOU ARE GOING TO COME UP WITH GUIDELINES FOR HORMONE TREATMENT FOR THOSE WOMEN THAT ARE GOING TO BE QUITE DIFFERENT FROM THE ONES THAT ARE DONE IN SOME OF THE INFERTILITY CLINICS. THE WHOLE DEMOGRAPHICS OF THOSE FOLKS, I THINK, ARE GOING TO BE DIFFERENT. AND SO I WOULD REALLY THINK IT WOULD BE -- I CERTAINLY THINK YOU ARE GOING TO BE ABLE TO COME UP WITH ADVERSE OUTCOMES. FROM WHAT BOB'S TALKING ABOUT, I'M NOT SURE THAT PEOPLE GOING THROUGH THIS FOR RESEARCH PURPOSES WOULD BE EXPOSED TO THAT KIND OF RISK ANYWAY. I THINK IT'S LIKE A WHOLE DIFFERENT SET OF LADIES AND A DIFFERENT KETTLE OF FISH. YOU COULD CERTAINLY FROM THAT DATABASE COME UP WITH WHAT NOT TO DO PERHAPS.

DR. TAYLOR: THAT'S WHAT I'M THINKING BECAUSE THE NUMBERS OF SUBJECTS THAT WE'LL HAVE IN DONATION FOR RESEARCH PURPOSES, THAT'S A WONDERFUL LONG-TERM STUDY, BUT I THINK TO COME UP WITH GUIDELINES THAT WOULD INFORM US ABOUT POTENTIAL RISKS, I JUST THINK IT'S GOING TO TAKE US TOO LONG TO GET THE INFORMATION. I AGREE IT'S A VERY CONSERVATIVE GROUP IN A WAY BECAUSE I THINK WE'LL OVERESTIMATE THE RISK THAT THOSE SUBJECTS WOULD BE EXPOSED TO, BUT I'D RATHER OVER THAN UNDERESTIMATE THAT RISK.

CHAIRMAN LO: IT STRIKES ME ALSO THAT THERE

ARE SOME OTHER ISSUES WE SHOULD THINK ABOUT. ONE IS LONG-TERM FOLLOW-UP. DO WE WANT TO FOLLOW THESE PEOPLE, GET PERMISSION AT THE TIME THEY AGREE TO BE OOCYTE DONORS, TO FOLLOW THEM UP FOR MANY YEARS TO SEE WHAT HAPPENS DOWN THE ROAD?

DR. KIESSLING: MAYBE WE SHOULD JUST COLLECT EGGS FROM NURSES, THE NURSES STUDY.

CHAIRMAN LO: THEY REPORT. THE OTHER QUESTION IS I GUESS THERE ARE GOING TO BE OTHER STATES THAT ARE GOING TO BE TRYING TO DO THIS, RIGHT? MASSACHUSETTS, IF I CAN TRUST THE NEWSPAPERS. ONE QUESTION WOULD BE IS CIRM INTERESTED IN TRYING TO -- THIS IS REALLY SORT OF HYPOTHETICAL -- COLLABORATING WITH OTHER STATES WHO ARE ALSO FUNDING STEM CELL RESEARCH AND OOCYTE DONATION FOR RESEARCH AND DOING SOME INTRASTATE. I'M WONDERING, IT SEEMS LIKE WE HAVE SOME IDEAS, BUT WE MAY NEED MORE SORT OF RESEARCH DESIGN BY A STATISTICS INPUT TO SAY HOW MANY PEOPLE, BUT MAYBE WHAT WE SHOULD DO IS SORT OF TRY AND MAKE A RECOMMENDATION THAT A GROUP WITHIN CIRM SORT OF REALLY PUSH THIS AS PART OF, AGAIN, A SMALL WORKING GROUP TO SORT OF SAY LET'S DEVELOP AN RFA THAT REALLY ADDRESSES THIS PROBLEM AND DOES IT IN A COMPREHENSIVE WAY.

MR. SHEEHY: MAYBE YOUR CONSULTING GROUP MIGHT NOT BE A BAD BODY TO DEVELOP THE RFA BECAUSE THEY

ACTUALLY WOULD HAVE THE EXPERTISE. ONE WITH SPECIALIZED EXPERTISE, I THINK, IF YOU PICK THAT GROUP THE WAY THAT YOU ARE DESCRIBING IT, THEY COULD PROBABLY COME UP WITH AN RFA, AND THAT WOULD PROBABLY BE THE BEST GROUP TO DESCRIBE AN RFA.

CHAIRMAN LO: IT MAY NEED --

MR. SHEEHY: IF IT'S DESIGNED RIGHT, OTHER GROUPS COULD POSSIBLY BUY IN AS TIME GOES ON.

CHAIRMAN LO: IT MAY NEED PEOPLE WHO ARE RESEARCH EPIDEMIOLOGY BIOSTATISTICS TYPES. I LIKE THIS NOTION OF TRYING TO GET SYNERGY BETWEEN THE DIFFERENT GROUPS.

MR. SHEEHY: THESE PIECES CAN WORK TOGETHER ACTUALLY. BESIDES JUST LOOKING AT CALIFORNIA, THEY MAY HAVE OTHER DATA SETS THAT THEY THINK MIGHT BE INTERESTING TO INCLUDE IN THE MIX TO GET THE DIVERSITY OF DATA THAT WE NEED.

DR. TAYLOR: I WAS JUST MORE CONCERNED ABOUT HOW BROADLY CIRM WAS INTERESTED IN SPREADING ITS FUNDS.

MR. SHEEHY: ULTIMATELY THE GOAL HERE IS PATIENT SAFETY OR DONOR SAFETY.

CHAIRMAN LO: OR WE COULD DO IT IN A TWO-STAGE, SEVERAL STAGE PROCESS. FIRST, GIVE US SOME BEST PRACTICE GUIDELINES; AND THEN IF YOU'RE STILL STANDING AND HAVE THE ENERGY, HELP US THINK THROUGH HOW

TO GET BETTER DATA. AND IT MAY NOT BE ALL THE SAME MEMBERS, BUT AT LEAST WE MIGHT HAVE A CORE.

DR. KIESSLING: EGG SHARING IS OFF THE TABLE? HOW IS THIS GOING TO RELATE TO -- THAT'S A VERY POPULAR THING GOING ON IN ENGLAND RIGHT NOW.

CHAIRMAN LO: GEOFF, YOU'VE TALKED A LOT WITH THE BRITS ABOUT THIS, OUR COLLEAGUES IN THE UK.

DR. LOMAX: SO THE QUESTION IS OF SERVICE FOR EGGS. AT THE MOMENT THE WAY OUR REGULATIONS ARE CONSTRUCTED, WE DON'T DO THAT.

DR. KIESSLING: WELL, SETTING ASIDE THE WHOLE CONCEPT OF REIMBURSEMENT, WHAT THEY'RE DOING IN ENGLAND IS THEY'RE ASKING WOMEN TO DONATE SOME OF THEIR EGGS FOR RESEARCH PURPOSES THAT ARE GOING THROUGH INFERTILITY TREATMENT, AND THEY'RE STRUGGLING WITH THE CONSENT FORMS TO DO THAT. SOME AREAS THEY'RE HOPING THAT THIS WILL KIND OF OFFSET THE COSTS OF THEIR OWN IVF CYCLES. WE'VE JUST BEEN ASKED BY THE HARVARD PROVOST TO LOOK AT THAT AND SEE WHAT'S WRONG WITH EGG SHARING AT HARVARD'S ESCRO. AND I KNOW THAT WE'VE TALKED ABOUT IT BEFORE. I DON'T KNOW IF IT'S BEEN TOTALLY REJECTED AS A CONCEPT.

DR. LOMAX: THERE'S TWO POINTS. FIRST OF ALL, WE DID CONTACT HFEA. AND IT'S STILL A WORK IN PROGRESS IN TERMS OF -- THEY'RE GETTING DOWN TO THE

LEVEL OF, AS I UNDERSTAND IT, WHAT, FOR EXAMPLE, IF YOU HAVE AN EGG SHARING ARRANGEMENT, WHAT COSTS ACTUALLY ARE ELIGIBLE. THAT'S A WORK IN PROGRESS, AND WE'RE WAITING TO SEE WHAT THEIR POLICY LOOKS LIKE. IT'S VERY DIFFICULT TO IMAGINE HOW ANY SCENARIO THAT SORT OF FALLS UNDER THE RUBRIC OF EGG SHARING WOULD NOT TRIGGER OUR VALUABLE CONSIDERATION TRIGGER IN OUR REGULATIONS. SO WHILE WE'RE PAYING ATTENTION TO IT, IT'S CERTAINLY NOT A POLICY THAT IN MY DISCUSSIONS WITH COUNSEL, SO YOU SORT OF SEE SOME SORT OF CARRY-OVER THAT WE WOULD HAVE SORT OF AN EQUIVALENT ARRANGEMENT HERE.

DR. KIESSLING: SO SETTING ASIDE WHETHER OR NOT IT WOULD HELP THEM COVER THEIR COST OF INFERTILITY, ARE CLINICS BEING APPROACHED? IS ANYBODY THINKING OF ORGANIZING CONSENT FORMS SO THAT YOU WOULD TALK TO A WOMAN WHO'S ABOUT TO GO THROUGH AN IVF, AND WOULD SHE LIKE TO DONATE TWO OF HER EGGS TO RESEARCH INDEPENDENT AND NOT HAVE THAT HAVE ANYTHING TO DO WITH THE COST OF HER TREATMENT? HAS THAT JUST BEEN TOTALLY SET ASIDE?

CHAIRMAN LO: AGAIN, TO GO BACK TO WHEN WE DEVELOPED THE REGULATIONS, WE TALKED ABOUT NOT COMPROMISING THE REPRODUCTIVE INTERESTS OF THE WOMAN UNDERGOING FERTILITY TREATMENT. SO I THINK IT DOESN'T RULE THAT OUT, BUT WE HAVE TO REALLY SORT OF -- I THINK -- AS I REMEMBER GOING THROUGH THE MINUTES OF

THOSE MEETINGS, WE WANTED TO SET A HIGH BAR OF SORT OF WHAT DOES IT MEAN TO SORT OF LOWER YOUR REPRODUCTIVE PROBABILITY?

DR. LOMAX: THAT'S CORRECT. I WAS JUST TRYING -- THANK YOU FOR JUMPING IN THERE, BERNIE. THAT'S RIGHT. WE SORT OF TRIED TO BREAK THIS DOWN, AND BOTH THE VALUABLE CONSIDERATION TRIGGER AND THE OPTIMAL REPRODUCTIVE SUCCESS TRIGGER IN OUR REGULATIONS, IT SEEMS TO VIOLATE BOTH THOSE AT FACE VALUE. AND SO THAT'S WHERE, I THINK, THE IDEA THAT THIS WOULD BE PRACTICED IN CALIFORNIA IS UNLIKELY.

DR. PETERS: COULD I JUST ASK JEFF A FACTUAL QUESTION? IN THE APPLICATIONS FOR SCNT EXPERIMENTATION, WERE THEY ALL FRESH EGGS, OR WERE SOME OF THOSE FROZEN EGGS IN THOSE PROTOCOLS?

MR. SHEEHY: I DID NOT SEE THE ONE. ONE OF THEM I DID NOT SEE, SO I HAVE NO INFORMATION ON IT. THE OTHER ONE WAS WITH FROZEN EGGS, WHICH RAISED SOME OF MY CONCERNS. I WONDER WHAT KIND OF INFORMED CONSENT HAD BEEN PUT IN PLACE, IF THERE HAD EVEN BEEN INFORMED CONSENT. SOMEBODY COULD JUST GO IN THE FREEZER AND TAKE SOMETHING OUT. AND LOOKING AT THE APPLICATION, THERE WAS ABSOLUTELY NO INFORMATION ABOUT THE PROCESSES BY WHICH THESE EGGS HAD BEEN OBTAINED. THERE WAS -- THE REVIEW ENTITY WAS A PRIVATE IRB. IT WASN'T AN

INSTITUTIONAL IRB, AND THERE WAS NO SCRO REVIEW THAT HAD TAKEN PLACE. SO THAT ONE MADE ME FEEL A LITTLE UNCOMFORTABLE.

DR. KIESSLING: EGG FREEZING IS GETTING BETTER AND EASIER AND MORE EFFICIENT, SO THAT'S ACTUALLY GOING TO CHANGE THIS CONVERSATION QUITE A BIT.

WOULD IT BE USEFUL FOR THIS OVERSIGHT COMMITTEE OR WHOEVER GROUP TO TALK ABOUT WHAT KIND OF INFORMED CONSENT YOU NEED FOR THESE PATIENTS?

CHAIRMAN LO: I THINK THAT'S -- AS WE LOOK AHEAD TO SORT OF WHAT SHOULD BE ON OUR AGENDA, I THINK WHAT YOU ARE SUGGESTING IS THAT SHOULD BE SOMETHING THAT WE CONSIDER. AND I GUESS CERTAINLY I WOULD DEFER TO ROB. MY IMPRESSION IS THE SCIENCE IS GETTING BETTER, OOCYTE FREEZING IS BECOMING MORE WIDELY AVAILABLE, AND SO --

DR. PETERS: ARTICLES IN *SCIENCE* MAGAZINE; APRIL 20 ON JUST THAT TOPIC.

CHAIRMAN LO: IT DOES OFFER A WAY OF GETTING AROUND COMPROMISING THE REPRODUCTIVE SUCCESS OF THE WOMAN IN IVF BECAUSE YOU CAN FREEZE SOME OOCYTES RATHER THAN FREEZING EMBRYOS. AND IF YOU'VE COMPLETED YOUR FAMILY, OKAY, NOW I DON'T NEED THOSE OOCYTES, TEN YEARS AGO I WOULD SAY I DON'T NEED THOSE, AND I DON'T WANT TO GIVE THEM TO ANOTHER WOMAN FOR HER REPRODUCTIVE USES.

I'D RATHER INSTEAD GIVE THEM TO RESEARCH.

IT STRIKES ME THAT WOULD ADDRESS A LOT OF CONCERNS ABOUT DIVVYING UP, LIKE DEALING OUT FRESH OOCYTES, ONE FOR ME, ONE FOR THE RESEARCHERS. THAT'S A BIT ODD. IF YOU THINK THAT'S A REAL UP AND COMING THAT WE SHOULD ADDRESS AND ISN'T COVERED -- I GUESS THE OTHER THING IS THE ETHICAL ISSUES AREN'T COVERED IN OUR CURRENT REGULATIONS. ARE THERE SPECIFIC THINGS ABOUT FROZEN OOCYTES THAT WE HAVEN'T ADDRESSED? AND MAYBE IT JUST MEANS WE NEED TO LEARN MORE ABOUT IT AND THINK IT THROUGH AND, AS PAT SUGGESTED, SEE A COUPLE OF ACTUAL PROTOCOLS. THAT MAY BE SOMETHING THAT WILL BE WELL WORTH OUR DOING.

I THINK YOU'RE RIGHT. ANN AND TED AND ROB HAVE SAID THIS IS GOING TO BE HAPPENING MORE AND MORE. DO WE HAVE THINGS IN PLACE?

DR. LOMAX: CERTAINLY JUST TO ANSWER YOUR QUESTION, AGAIN A FACE-VALUE READ OF THE REGULATIONS, IF THOSE OOCYTES ARE TAKEN FROM THE FREEZER WITH THE INTENT OF DERIVING A STEM CELL LINE, THEN OUR REGULATIONS ARE INTACT. SO THE QUESTION SIMPLY BECOMES THE ADEQUACY OF THE REGULATIONS, NOT WHETHER THAT CIRCUMSTANCE IS ADDRESSED BY THE REGULATIONS. SO WE CERTAINLY, I THINK, IN TERMS OF HOW WE CAST THE REGULATIONS, I JUST WOULD LIKE TO REMIND THE WORKING

GROUP THAT THE INTENT TO DERIVE A CELL LINE TRIGGERS ESSENTIALLY THE ENTIRE CONSENT PROCESS. SO THE QUESTION MAY BECOME ONE OF THEN THE ADEQUACY OF THAT PROCESS; HOWEVER, IT IS TRIGGERED BY VIRTUE OF THE DERIVATION PROTOCOL.

CHAIRMAN LO: JUST TO FOLLOW THAT UP, THERE ARE TWO SITUATIONS. ONE IS AN OOCYTE DONOR PROVIDES OOCYTES PRIMARILY WITH THE INTENT FOR IVF, SOME ARE FROZEN AND END UP NOT BEING USED. THE OOCYTE DONOR WOULD HAVE TO CONSENT AS WELL AS THE IVF PATIENT TO WHOM THE OOCYTES WERE GIVEN; IS THAT CORRECT?

DR. LOMAX: AND, AGAIN, THAT IS ADDRESSED IN REGULATIONS. WE DO REQUIRE CONSENT FROM ALL GAMETE DONORS. SO, YES. SHORT ANSWER TO THE QUESTION IS YES.

CHAIRMAN LO: SO I GUESS THE OTHER QUESTION IS THE PAYMENT. IF YOU GOT PAID TO DONATE OOCYTES FOR CLINICAL IVF, BUT IT ENDS UP YOU DON'T NEED THOSE OOCYTES, JUST AS THEY'D GONE INTO EMBRYOS AND DON'T NEED THEM, SO WHERE DO WE STAND ON CONSIDERATION FOR THAT?

DR. LOMAX: I WILL REMIND THE COMMITTEE OF THE JULY 17TH CONFERENCE CALL. THE CLOSEST WE GOT TO THIS ISSUE WAS DISCUSSION OF FAILED-TO-FERTILIZE OOCYTES THAT CAME FROM PAID DONORS. THE SENSE OF THE COMMITTEE AT THAT TIME WAS THAT BY VIRTUE OF PAYMENT,

THE OOCYTES SHOULD NOT BE ALLOWED FOR DERIVATION; AND SO, THEREFORE, THE INTERPRETATION AT THIS TIME IS ANY PAID OOCYTE WOULD NOT BE USED FOR CIRM-FUNDED RESEARCH. THE ISSUE HAS EMERGED IN SOME OF THE FACT-FINDING I'VE DONE PURSUANT TO OUR EVALUATION INITIATIVE, AND THIS IS IN THE CONTEXT OF EMBRYOS, AND WE CAN BRING THAT UP TOMORROW BECAUSE I THINK IT WILL COME UP IN A MORE HOLISTIC CONTEXT AT THAT TIME.

CHAIRMAN LO: OKAY. SO WHERE ARE WE NOW? CAN I TRY AND MAKE A WILD STAB HERE AT TRYING TO CLOSE THIS DOWN? LET ME TRY THREE THINGS. ONE IS THAT WE AUTHORIZE, I GUESS, MAYBE ME AND GEOFF AND CIRM STAFF TO PROCEED FURTHER IN CONVENING A GROUP OF --

DR. LOMAX: CAN I INTERRUPT YOU THERE? I SEE SCOTT WAVING A FINGER, SO MY SENSE IS THERE MAY BE SOME CONCERN ABOUT THE NATURE --

MR. TOCHER: I JUST WANTED TO CLARIFY FOR A MOMENT THAT, FIRST OF ALL, JUST TO STEP BACK, PROCESS ISSUES, WE DON'T HAVE A QUORUM PRESENT FOR THE GROUP. SO THE GROUP WON'T BE TAKING ANY OFFICIAL ACTION, JUST IN GENERAL.

CHAIRMAN LO: IT'S A SENSE OF THE COMMITTEE.

MR. TOCHER: THAT'S RIGHT.

DR. KIESSLING: WILL WE HAVE A QUORUM TOMORROW?

CHAIRMAN LO: NO. WE GOING TO HAVE A QUORUM TOMORROW? NO.

MR. TOCHER: THAT DOESN'T RENDER IT USELESS WHAT YOU ARE DOING BECAUSE, TO MY SECOND POINT, WE'RE NOT ACTUALLY LOOKING FOR THE COMMITTEE TO AUTHORIZE OR CREATE THIS GROUP OF EXPERTS AND CONSULTANTS TO GATHER THIS DATA, BUT RATHER TO, I THINK, ASSIST GEOFF AND CIRM STAFF IN DIRECTING THE WORK OF THAT GROUP SO THAT WHEN IT COLLECTS THE DATA, IT'S COLLECTING DATA AND PERFORMING AN ANALYSIS THAT IT BRINGS TO YOU AND, WHERE POSSIBLE, FORMULATE RECOMMENDATIONS SO THAT IT'S HELPFUL FOR YOU WHEN YOU DECIDE WHICH RECOMMENDATIONS YOU WANT TO BRING FORTH TO THE ICOC.

AND THE REASON FOR THIS, I WON'T GO INTO IT, BUT JUST FOR A BUNCH OF BUREAUCRATIC RULES, THIS MAKES THIS THE MOST EFFICIENT METHOD POSSIBLE FOR COLLECTING THIS INFORMATION AND CONSOLIDATING IT FOR YOUR USE. AND ONE OF THE DISTINCTIONS THERE THAT'S IMPORTANT TO MAKE, THEN, IS THAT YOU'RE NOT AUTHORIZING IT TODAY. IT'S NOT BEING CREATED BY YOU, BUT RATHER IS A CREATION BY CIRM STAFF AS A TOOL FOR STAFF FOR THE COMMITTEE.

CHAIRMAN LO: HELP ME OUT HERE. IS THE SENSE -- WE'D LIKE TO FIND OUT WHETHER IT IS THE SENSE OF THE COMMITTEE THAT, AND YOU GUYS HAVE TO HELP ME, THE SENSE OF THE COMMITTEE AND GEOFF THAT CIRM STAFF --

MR. TOCHER: THAT IT WOULD BE HELPFUL IF GEOFF WERE ABLE TO BRING BACK, YOU KNOW, AN ANALYSIS OR RECOMMENDATIONS REGARDING THESE SPECIFIC AREAS THAT YOU'RE TALKING ABOUT.

CHAIRMAN LO: IT'S THE SENSE OF THE COMMITTEE THAT IT WOULD BE HELPFUL IF GEOFF AND STAFF WOULD OBTAIN FROM EXPERT CONSULTANTS BEST PRACTICE INTERIM GUIDELINES ON HOW TO MINIMIZE RISKS TO OOCYTE DONORS FOR RESEARCH WITH A PARTICULAR VIEW TOWARDS GETTING INFORMATION ON MAKING RECOMMENDATIONS ON HOW TO MINIMIZE RISKS FOR MINORITY WOMEN AND OTHER WOMEN WHO ARE NOT REPRESENTED IN THE DATABASE OF CURRENT STUDIES BY INCLUDING PEOPLE -- BY INCLUDING AMONG THOSE CONSULTANTS PEOPLE WITH EXPERIENCE WITH SUCH POPULATIONS. IS THAT SORT OF WHAT --

DR. TAYLOR: PERIOD.

CHAIRMAN LO: ALL RIGHT. SO WE'RE NOT DOING MOTIONS. I GUESS I JUST SORT OF WANT TO GET A SENSE. IS THAT A SENSE?

DR. PETERS: THAT'S THE SENSE. JUST ONE CLARIFICATION. THEY WOULD PROVIDE DATA FOR US TO COME UP WITH INTERIM GUIDELINES. THEY WOULDN'T DO IT FOR US, RIGHT?

CHAIRMAN LO: THEY MIGHT RECOMMEND -- I THINK THEY MIGHT RECOMMEND TO US WHAT THEY THINK GUIDELINES

MIGHT LOOK LIKE.

DR. PETERS: BUT THEY WOULD BE OUR GUIDELINES.

CHAIRMAN LO: WE WOULD NEED -- AND THAT WOULD BE A PUBLIC PROCESS. I THINK WE WOULD WANT, THEN, TO HAVE PEOPLE LIKE THE PEOPLE HERE TODAY WHO HAVE COMMENTED. SO IT'S REALLY ADVISORY.

MR. TOCHER: ADVISORY TO STAFF.

CHAIRMAN LO: ADVISORY TO STAFF. THANK YOU. SO THAT'S ONE.

THE SECOND IS LET ME MAKE ANOTHER. IS IT THE SENSE OF THIS COMMITTEE THAT -- WELL, I GUESS MAYBE WE SHOULD TRY TOMORROW TO COME BACK TO THIS QUESTION OF HOW WE SHOULD GET INVOLVED WITH PROTOCOLS THAT COME ACROSS CIRM THAT RAISE ETHICAL CONCERNS BOTH FOR OUR OWN EDUCATION AND ALSO TO PERHAPS ADD TO THE REVIEW AND REVISION PROCESS. AND IT SOUNDS LIKE MAYBE WE COULD SORT OF COGITATE ON THAT OVERNIGHT AND COME UP WITH THAT TOMORROW.

AND THE THIRD THING, AGAIN I WOULD SUGGEST WE TRY AND THINK ABOUT IT OVERNIGHT, IS TRYING TO -- AGAIN, TOMORROW TRY AND COME UP WITH WHAT'S THE SENSE OF THIS COMMITTEE WITH REGARD TO GETTING CIRM INVOLVED IN SENDING OUT AN RFP FOR BETTER AND MORE COMPREHENSIVE AND MORE REPRESENTATIVE DATA ON THE RISKS OF OOCYTE

DONATION FOR RESEARCH?

MR. SHEEHY: I JUST WONDER IF WE COULD ADD A LITTLE FRIENDLY AMENDMENT, WHICH IS ANN KIESSLING'S RECOMMENDATION, THAT WE ACTUALLY COLLECT DATA ON THE DONORS THAT WE FUND AS PART OF THAT RFA BECAUSE WE REALLY SHOULD BE COLLECTING DATA ON ANY. THAT COULD BE --

DR. KIESSLING: YOU NEED TO DO A DONOR REGISTRY. THAT WOULD JUST BE FABULOUS.

CHAIRMAN LO: DONOR REGISTRY OF WOMEN DONATING --

DR. KIESSLING: THEY SHOULD BE ANONYMOUS.

DR. ROWLEY: IF IT'S ANONYMOUS, YOU WILL NEVER BE ABLE TO -- I WON'T SAY NEVER -- BUT THE DATA REALLY THEN BECOME VERY LIMITED. IT SHOULD BE PRIVACY PROTECTED. I'M ALL IN FAVOR OF THAT, BUT NOT ANONYMOUS.

CHAIRMAN LO: THERE ARE -- AGAIN, I THINK THERE ARE WAYS OF CRAFTING IT SO THAT WE TRY AND OBTAIN LONG-TERM FOLLOW-UP CONSISTENT WITH PROTECTING THE PRIVACY AND CONFIDENTIALITY OF --

DR. KIESSLING: I THINK THE DONORS PROBABLY JUST DON'T WANT TO APPEAR AS A LIST IN THE *L.A. TIMES* SOMEDAY.

MR. SHEEHY: YOU COULD DO A UNIQUE IDENTIFIER

SYSTEM.

CHAIRMAN LO: ALL RIGHT. HAVING REACHED THIS POINT, IS IT THE SENSE AND PLEASURE OF THE COMMITTEE THAT WE ADJOURN FOR THE EVENING?

MS. KING: YES.

CHAIRMAN LO: AND TRY AND FIND SOME DINNER?

MS. KING: YES.

CHAIRMAN LO: SOMEONE WANT TO MOVE THAT WE -- WE CAN'T DO ANYTHING. I CAN DO WHATEVER I WANT. IT'S CLEARLY THE SENSE OF THE COMMITTEE. GREAT. SO THANK YOU VERY MUCH. AND THEN LET'S GO HAVE DINNER, AND THEN WE'RE GOING TO RECONVENE HERE AT 8:30 TOMORROW.

DR. LOMAX: WE ARE SCHEDULED FOR 8 O'CLOCK. DO WE WANT TO TRY FOR 8:00 OR 8:30?

CHAIRMAN LO: SO IS IT THE SENSE OF THE COMMITTEE, YOU WANT TO START AT 8:00 OR 8:30? THE SOONER THE START, THE SOONER WE FINISH. WHAT YOU ARE REALLY DOING IS ALLOWING THOSE IN SAN FRANCISCO --

DR. LOMAX: WE WERE ANTICIPATING FINISHING AROUND NOON.

CHAIRMAN LO: DOES IT MATTER TO ANYBODY?

DR. PETERS: I PREFER 8:30, BUT I'LL MAKE IT 8 O'CLOCK.

CHAIRMAN LO: ANYONE HAVE A STRONG FEELING FOR MAKING IT EIGHT? IF NOT, HOW ABOUT 8:30? ARE WE

ALLOWED TO DO THAT BECAUSE WE PUBLICLY ANNOUNCED?

MR. TOCHER: THE ONLY PROBLEM WOULD BE IF YOU WERE TRYING TO MOVER IT EARLIER. IT JUST MEANS PEOPLE WOULD COME HERE AND COOL THEIR HEELS FOR A WHILE.

CHAIRMAN LO: THANK YOU VERY MUCH.

(THE MEETING WAS THEN RECESSED AT 07:39 P.M. TO RECONVENE AT 8:30 A.M. ON MAY 10TH, 2007.)

REPORTER'S CERTIFICATE

I, BETH C. DRAIN, A CERTIFIED SHORTHAND REPORTER IN AND FOR THE STATE OF CALIFORNIA, HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT OF THE PROCEEDINGS BEFORE THE SCIENTIFIC AND MEDICAL ACCOUNTABILITY STANDARDS WORKING GROUP OF THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD AT THE LOCATION INDICATED BELOW

MIYAKO HOTEL
1625 POST STREET
SAN FRANCISCO, CALIFORNIA
ON
MAY 9, 2007

WAS HELD AS HEREIN APPEARS AND THAT THIS IS THE ORIGINAL TRANSCRIPT THEREOF AND THAT THE STATEMENTS THAT APPEAR IN THIS TRANSCRIPT WERE REPORTED STENOGRAPHICALLY BY ME AND TRANSCRIBED BY ME. I ALSO CERTIFY THAT THIS TRANSCRIPT IS A TRUE AND ACCURATE RECORD OF THE PROCEEDING.

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